(25.degree. C.), the organic solution was extracted with four volumes of 0.1% NaHCO.sub.3. The bicarbonate solution was slowly adjusted to pH 4.5 with ethyl acetate which was subsequently concentrated to 100 ml in vacuo. The concentrate was combined with 150 ml of diethyl ether containing an excess of CH.sub.2 N.sub.2 and stirred overnight for preparation of the methyl ester derivatives. Evaporation of the ether was performed under a stream of nitrogen and the remaining solution was washed with 100 ml of phosphate buffer, pH 7.0. The organic phase was taken to dryness in vacuo and the resulting residue was dissolved in a minimum of isopropanol. Final purification of methyl 7-[1,2,6,7,8,8a(R)-hexahydro-6(S)-hydroxymethyl-2(S)-methyl-8(S)-(2,2-dime thylbutyryloxy)-1(S)-naphthyl]-3(R),5(R)-dihydroxyheptanoate was accomplished by HPLC utilizing a Waters .mu.Bondapak-C18 column (1.times.30 cm). The mobile phase was 34 percent aqueous CH.sub.3 3 CN at 4 ml/min. Methyl 7-[1,2,6,7,8,8a(R)-hexahydro-6(S)-hydroxymethyl-2(S)-methyl-8 (S)-(2,2-dime thylbutyryloxy)-1(S)-naphthyl]-3(R),5(R)-dihydroxyheptanoate had a retention time at 31 minutes. After evaporation of the solvent, the sample was dried under vacuum for 24 hours to afford the title compound which was identified by NMR. 1.sub.H nmr (CDCl.sub.3) .delta. 0.83 (3H, t, J=7 Hz), 0.89 (3H, d, J=7Hz), 1.107 (3H, s), 1.111 (3H, s), 2.16 (H, m), 3.51 (H, d of d, J=5.5, 10.5 Hz), 3.61 (H, d of d, J=5.5, 10.5 Hz), 3.69 (3H,s), 3.77 (H, m), 4.22 (H, m) 5.36 (H, bs), 5.50 (H, bs), 5.80 (H, d of d, 6, 9.5 Hz), 6.00 (H, d, J=9.5 Hz).

IV. Isolation of 6(R)-[2-[8(S)-(2,2-Dimethylbutyryloxy)-6(R)-carboxy-2(S)-methyl-1,2,6,7,8, 8a(R)-hexahydronaphthyl-1(S)]ethyl]-4(R)-hydroxy-3,4,5,6-tetrahydro-2H-pyra n-2-one and 6(R)-[2-(8(S)-(2,2-Dimethylbutyryloxy)-6(S)-carboxy-2(S)-methyl-1,2,6,7,8, 8a(R)-hexahydronaphthyl-1(S)]ethyl]-4 (R)-hydroxy-3,4,5,6-tetrahydro-2H-pyra n-2-one.

The whole broth (1200 ml) was clarified as before and then adjusted to pH 3.5 with H.sub.3 PO.sub.4. The filtrate was loaded on a HP-20 column (3.times.50 cm) which had been equilibrated with water containing 0.1 percent CH.sub.3 COOH. After washing the column with 1 L of water and 1 L of 25 percent CH.sub.3 CN, the products were eluted with 600 ml of 50 percent CH.sub.3 CN. The acetonitrile was removed under vacuum at 35.degree. C. The water was taken to pH 8.0 with NaOH and washed with two 500 ml portions of CH.sub.2 Cl.sub.2 which was discarded. After readjusting the pH to 3.5 with H.sub.3 PO.sub.4, the derivatives were first extracted into 1.8 L ethyl acetate and then back-extracted into 1 L of 1 percent NaHCO.sub.3. The bicarbonate solution was acidified to pH 5 with acetic acid and loaded on a HP-20 column (1.5.times.50 cm). Once the column was washed with 700 ml of H.sub.2 O followed by 700 ml of 30 percent CH.sub.3 CN, the column was eluted with a gradient of 30 to 50 percent CH.sub.3 CN. The fractions were monitored by UV absorbance (228, 238, 248 nm) and by HPLC. Crude 6(R)-[2-[8(S)-(2,2-dimethylbutyryloxy)-6(S)-carboxy-2(S)-methyl-1,2,6,7,8, 8a(R)-hexahydronaphthyl-1(S)]ethyl]4(R)-hydroxy-3,4,5,6-tetrahydro-2H-pyran -2-one was collected at about 40 percent CH.sub.3 CN.

After removing the solvent in vacuo, the resulting residue was sonicated with 20 ml of toluene for 10 minutes, 3 .mu.l of CF.sub.3 COOH was added and the mixture was heated for 30 minutes at 70.degree. C. The toluene was removed under vacuum at 70.degree. C. and the resulting residue was dissolved in 300 .mu.l of CH.sub.3 CN. The preceding procedure was employed to convert the derivative of 7-[1,2,6,7,8,8a(R)-hexa- hydro-2(S),6(R)-dimethyl-(b 2,2-dimethylbutyryloxy)-1(S)-naphthyl]-3(R),5(R)-dihydroxyheptanoic acid to its lactone form for ease of isolation. Final purification was accomplished by HPLC using an Altex-C8 column (1.times.25 cm) and a gradient of CH.sub.3 CN/CH.sub.3 OH/H.sub.2 O/CH.sub.3 COOH (20/30/50/0.01 to 25/30/45/0.01) at 2.7 ml/min. 6(R)-[2-[8(S)-(2,2-Dimethylbutyryloxy)-6(S)-carboxy-2(S)-methyl-1,2,6,7,8, 8a(R)-hexahydronaphthyl-1(S)]ethyl]-4(R)-hydroxy-3,4,5,6-tetrahydro-2H-pyra n-2-one had a retention time of 30 to 31 minutes and was identified by NMR. 1.sub.H nmr (CDCl.sub.3) .delta. 0.82 (3H, t, J=7.5 Hz), 0.88 (3H, d, J=7 Hz), 1.11 (6H, s), 1.53 (H, m), 2.60 (H, m) 2.72 (H, d of d, J=5, 18 Hz), 3.29 (H, m), 4.365 (H, m), 4.60 (H, m), 5.39 (H, bs), 5.62 (H, bs), 5.83 (H, d of d, J=6, 10 Hz), 6.00 (H, d, J=10 Hz)

An alternate final purification involved fractionation by preparative HPLC using a Vydac C-18 column and eluting with 0-60% CH.sub.3 CN/0.170 phosphoric acid. Application of this purification technique to a partially-purified mixture of acidic materials (200 mg) afforded fractions A containing a less polar, major component and fractions B containing a more polar, minor component. Concentration of fractions A in vacuo to remove the bulk of the CH.sub.3 CN gave an aqueous mixture which was extracted with chloroform. The organic extract was washed with saturated brine, dried (Na.sub.2 SO.sub.4), filtered and evaporated in vacuo to provide 6(R)-[2-[8(S)-(2,2-dimethylbutyryloxy)-2(S)-methyl-6(S)-carboxy-1,2,6,7,8, 8a(R)-hexanaphthyl-1(S)]ethyl]-4(R)-hydroxy-3,4,5,6-tetrahydro-2H-pyran-2-o ne as a colorless solid, mp 167.degree.-170.degree. C.; 1.sub.H nmr (CD.sub.3 CN) .delta. 6.04 (H, d, J=9.8 Hz), 5.88 (H, d of d, J=9.7, 6.0 Hz), 5.62 (H, m), 5.33 (H, m), 4.56 (H, m), 4.23 (H, m), 3.23 (H, m), 2.62 (H, d of d, J=17.4, 4.8 Hz), 2.44 (H, d of d of d, J=17.5, 3.7, 1.6 Hz), 1.12 (6H, s), 0.90 (3H, d, J=7.1 Hz), 0.83 (3H, t, J=7.5 Hz). Recrystallization of this 6.beta.-carboxy isomer from EtoAc-Hexane did not alter the mp. Furthermore, this 6.beta.-carboxy isomer mp 167.degree.-170.degree. C., could be obtained directly from the partially-purified mixture of acidic materials (vida supra) by crystallization from di-n-butyl ether.

Anal. Calc'd for C.sub.25 H.sub.36 O.sub.7 : C, 66.94; H, 8.09. Found: C, 66.66; H, 8.41.

From fractions B (vida supra) there was obtained the corresponding 6.alpha.-carboxy isomer 6(R)-[2-[8 (S)-(2,2-dimethylbutyryloxy)-2-(S)-methyl-6(R)-carboxy-1,2,6,7,8 ,8a(R)-hexahydronaphthyl-1(S)] ethyl]-4(R)-hydroxy-3,4,5,6-tetrahydro-2H-pyr an-2one, as a colorless solid, mp 189.degree.-194.degree. C.; 1 H nmr (CD.sub.3 CN) .delta. 6.06 (H, d, J=9 Hz), 5.88 (H, d of d, J=9.5, 5.9 Hz), 5.71 (H, m), 5.24 (H, m), 4.51 (H, m), 4.21 (H, m), 3.20 (H, m), 2.70 (H, m), 2.62 (H, d of d, J=17.4, 4.8 Hz), 2.44 (H, m), 1.06 (H, s), 1.03 (3H, s), 0.89 (3H, d, J=7.0 Hz), 0.82 (3H, t, J=7.5 Hz).

Anal Calc'd for C.sub.25 H.sub.36 O.sub.7 : C, 66.94; H, 8.09. Found: C, 66.70; H, 8.38.

In a similar fashion Nocardia autotrophica subsp. canberrica ATCC 35203 (MA6181) was utilized in the bioconversion reaction with the sodium salt of 7-[1,2,6,7,8,8a(R)-hexahydro-2(S),6(R)-dimethyl-8(S)-(2,2-dimethylbutyr yloxy)-1(S)-naphthyl]-3(R),5(R)-dihydroxyheptanoic acid to afford the desired products.

Additionally, the sodium salt of 7-[1,2,6,7,8,8a(R)-hexahydro-2(S),6(R)-dimethyl-8(S)-(2-methylbutyryloxy)- 1(S)-naphthyl]-3(R),5(R)-dihydroxyheptanoic acid, the sodium salt of ring opened mevinolin, was subjected to analogous bioconversion reactions utilizing both N. autotrophic subsp. amethystina ATCC 35204 (MA6180) and N. autotrophic subsp. canberrica ATCC 35203 (MA6181) to predominantly afford 6(R)-[2-[8(S)-(2-methylbutyryloxy)-6(S)-carboxy-2(S)-methyl-1,2,6,7,8,8a(R)-hexahydronaphthyl-1(S)]ethyl]-4(R)-hydroxy-3,4,5,6-tetrahydro-2H-pyran-2- one and methyl 7-[1,2,6,7,8,8a(R)-hexahydro-6(S)-hydroxymethyl-2(S)-methyl-8(S)-(2-methyl butyryloxy)-1(S)-naphthyl]-3(R),5(R)-dihydroxyheptanoate, respectively.

EXAMPLE 2

Preparation of 6(R)-[2-[8(S)-(2,2-dimethylbutyryloxy)-2(S)-methyl-6(S)-hydroxymethyl-1,2, 3,4,4a (S),5,6,7,8,8a(S)-decahydronaphthyl-1(S)]ethyl]-4(R)-hydroxy-3,4,5,6- tetrahydro-2H-pyran-2-one

(a) 6(R)-[2-[8(S)-Nitrosyloxy-2(S),6(S)-dimethyl-1,2,3,4,4a(S),5,6,7,8,8a(S)-d ecahydronaphthyl-1(S)] ethyl]-4(R)-(tert-butyldimethylsilyloxy)-3,4.5.6-tetr ahydro-2H-pyran-2-one (2a)

A stream of nitrosyl chloride gas was passed into a stirred solution of 6(R)-[2-[8(S)-hydroxy-2(S), 6(S)-

dimethyl-1,2,3,4,4a(S),5,6,7,8,8a(S)-decahydro-naphthyl-1(S)]ethyl]-4 (R)-(tert-butyldimethylsilyloxy)-3,4,5,6-tetrahydro-2H-pyran-2-one (800 mg, 1.82 mmol) in pyridine (14 ml) at 0.degree. C. until the solution was saturated (brownish fumes filled the reaction flask). The resulting mixture was stirred at 0.degree. C. for another 10 minutes, poured into cold water and extracted with diethyl ether. The extract was washed successively with dilute HCl, water and 5% NaHCO.sub.3, dried (MgSO.sub.4), filtered and concentrated in vacuo to afford the title compound as a white solid; mp 92.degree.-4.degree. C.; 1.sub.H nmr (CDCl.sub.3) .delta. 0.86 (3H, d, J=7 Hz), 0.89 (9H, s), 0.99 (3H, d, J=7 Hz), 2.55 (H, m of d, J=18 Hz), 2.60 (H, d of d, J=18,4 Hz), 4.28 (H, m), 4.53 (H, m), 5.84 (H, m).

Anal Calc'd for C.sub.25 H.sub.45 NO.sub.5 Si: C, 64.20; H, 9.70; N, 3.00. Found: C, 64.09; H, 10.00; N, 3.06.

(b) 6(R)-[2-[8(S)-Hydroxy-2(S)-methyl-6(S)-nitrosylmethyl-1,2,3,4,4a(S),5,6,7, 8,8a(S)-decahydronaphthyl-1(S)]ethyl]-4(R)-(tert-butyldimethylsilyloxy)-3,4 ,5,6-tetrahydro-2H-pyran-2-one (2b)

Nitrogen gas was passed through a solution of compound 2a (870 mg, 1.82 mmol) in benzene (320 ml) for 25 minutes. This solution was irradiated under N.sub.2 with a 450 watt Hanovia medium pressure mercury lamp (pyrex filter) for 40 minutes at room temperature. The reaction mixture was then concentrated in vacuo and the residue applied to a silica gel column. Elution of the column with methylene chloride:acetone (50:1; v:v) followed by elution with methylene chloride:acetone: isopropanol (100:10:2; v:v:v) yielded the desired product as a foamy oil; 1.sub.H nmr (CDCl.sub.3) .delta. 0.83 (3H, d, J=7 Hz), 0.88 (9H, s) 4.10 (H, bs), 4.29 (H, m), 4.64 (2H, d, J=8 Hz), 4.67 (H, m).

(c) 6(R)-[2-[8(S)-Hydroxy-2(S)-methyl-6(S)-hydroxyiminomethyl-1,2,3,4,4a(S),5, 6,7,8,8a(S)-decahydronaphthyl-1(S)]ethyl]-4(R)-(tert-butyldimethylsilyloxy) -3,4,5,6-tetrahydro-2H-pyran-2-one (2c)

Compound 2b (288 mg, 0.616 mmol) was dissolved in isopropanol (15 ml) and heated at reflux for 2 hours. After cooling the reaction mixture was concentrated in vacuo to leave a residue which afforded the title compound as a gummy oil; 1.sub.H nmr (CDCl.sub.3) .delta. 0.86 (3H, d, J=7 Hz), 0.90 (9H, s) 2.33 (H, d, J=14 Hz), 2.78 (H, m), 4.11 (H, m), 4,32 (H, m), 4.66 (H, m), 7,50 (H, d, J=6 Hz).

(d) 6(R)-[2-[8-Hydroxy-2(S)-methyl-6(S)-formyl-1,2,3,4,4a(S),5,6,7,8,8a(S)-dec ahydronaphthyl-1(S)]-ethyl]-4(R)-(tert-butyldimethylsilyloxy)-3,4,5,6-tetra hydro-2H-pyran-2-one (2d)

Sodium nitrite (477 mg 6.83 mmol) was added at 0.degree. C. in one portion to a stirred solution of compound 2c (324 mg 0.683 mmol) in acetic acid (14 ml) and water (7 ml). The resulting mixture was stirred at 0.degree. C. for 10 minutes, warmed to room temperature and stirred for 2.5 hours. The mixture was then diluted with water and extracted with diethyl ether. This ethereal extract was washed with water, 5% NaHCO.sub.3 (twice), dried and filtered. Evaporation of the filtrate in vacuo afforded a brownish oily residue whose nmr spectrum is consistent with the structure for compound 2d; 1.sub.H nmr (CDCl.sub.3) .delta. 0.80 (3H, d, J=7 Hz), 0.88 (9H, s), 4,30 (H, m) 4.55 (2H, m).

(e) 6(R)-[2-[8(S)-Hydroxy-2(S)-methyl-6(S)-hydroxymethyl-1,2,3,4,4a(S),5,6,7,8 ,8a(S)-decahydronaphthyl-1(S)]ethyl]-4(R)-(tert-butyldimethylsilyloxy)-3,4, 5,6-tetrahydro-2H-pyran-2-one (2e)

Powdered sodium borohydride (40 mg, 1.05 mmol) was added at 0.degree. C. to a stirred solution of compound 2d (296 mg, 0.651 mmol) in 95% ethanol (15 ml) in one portion. The resulting mixture was

stirred at 0.degree. C. for 0.5 hours, then slowly treated with a solution of aqueous (NH.sub.4).sub.2 SO.sub.4 (0.7 g in 15 ml of H.sub.2 O). The resulting mixture was stirred at O.degree. C. for 0.5 hours, diluted with water (60 ml) and extracted with diethyl ether. This extract was washed with water, 5% NaHCO.sub.3, dried, filtered and evaporated to give a crude sample which was purified by flash chromatography. Elution of the column with methylene chloride:acetone:isopropanol (100:10:2; v:v:v) afforded the desired product as a white solid; mp 124.degree.-7.degree. C.; 1.sub.H nmr (CDCl.sub.3) .delta. 0.83 (3H, d, J=7Hz), 0.90 (9H, s), 3.73 (H, d of d, J=11,6 Hz), 3.79 (H, d of d, J=11,6 Hz), 4.10 (H, bs) 4.31 (H, m), 4.70 (H, m).

Anal Calc'd for C.sub.25 H.sub.46 O.sub.5 Si C, 66.03; H, 10.20. Found: C, 66.07; H, 10.38.

(f) 6(R)-[2-[8(S)-Hydroxy-2(S)-methyl-6(S)-(tert-butyldiphenylsilyloxymethyl)- 1,2,3,4,4a(S),5,6,7,8,8a (S)-decahydronaphthyl-l(S)]ethyl]-4(R)-(tert-butyld imethylsilyloxy)-3,4,5,6-tetrahydro-2H-pyran-2-one (2f)

A solution of tert butyldiphenylsilyl chloride (140 mg, 0.50 mmol) in dimethylformamide (1 ml) was added at 0.degree. C. to a stirred solution of compound 2e (0.150 g, 0.33 mmol) and imidazole (115 mg, 1.7 mmol) in dimethylformamide (4 ml). The resulting mixture was stirred at 0.degree. C. for 15 minutes and then warmed to room temperature and stirred for 15 hours. The mixture was poured into cold water and extracted with diethyl ether. This ethereal extract was washed with dilute HCl and 5% NaHCO.sub.3, dried, filtered and evaporated to leave crude product 2f which was purified by flash chromatography on a silica gel column. Elution of the column with methylene chloride:acetone (5:1; v:v) gave the desired product as a gummy oil; 1.sub.H nmr (CDCl.sub.3) .delta. 0.84 (3H, d, J=7 Hz), 0.90 (9H, s), 1.09 (9H, s), 2.99 (H, d, J=6 Hz), 3.7-3.85 (2H, m) 4.02 (H, m), 4.30 (H, m) 4.67 (H, m) 7,3-7.5 (6H, m), 7.65-7.8 (4H, m).

(g) 6(R)-[2-[8(S)-(2,2-Dimethylbutyryloxy)-2(S)-methyl-6(S)-(tert-butyldipheny lsilyloxymethyl)- 1,2,3,4,4a(S),5,6,7,8,8a(S)-decahydronaphthyl-1(S)]ethyl]- 4(R)-(tert-butyldimethylsilyloxy)-3,4,5,6-tetrahydro-2H-pyran-2-one (2g)

Lithium bromide powder (0.200 g, 2.30 mmol) was added at room temperature under N.sub.2 in one portion to a stirred solution of 2,2-dimethylbutyryl chloride (0.150 g, 1.11 mmol) in pyridine (3.5 ml). The resulting mixture was stirred at room temperature until it became a homogenous solution (0.5 hours). 4-Dimethylaminopyridine (DMAP) was added (80 mg, 0.65 mmol). To the resulting mixture was added a solution of compound 2f (229 mg, 0.33 mmol) in pyridine (2.5 ml). The resulting mixture as heated at 90.degree.-95.degree. under N.sub.2 for 70 hours. The reaction mixture was cooled, poured into cold water and extracted with diethyl ether. This ethereal extract was washed successively with dilute HCl, water and 5% NaHCO.sub.3, then dried, filtered and concentrated in vacuo to afford an oily residue which was purified by flash chromatography on silica gel, eluting with methylene chloride:acetone (200:1; v:v). The product fractions were purified further by preparative tlc (Analtech SiO.sub.2 plates, eluant=CH.sub.2 Cl.sub.2 :acetone (75:1; v:v) to give the desired compound as a colorless viscous oil; 1.sub.H nmr (CDCl.sub.3) .delta. 0.66 (3H, t, J=7 Hz), 0.84 (3H, d, J=7 Hz), 0.9 (9H, s). 0.91 (6H, s). 1.10 (9H, s) 3.51 (H, d of d, J=11,4 Hz) 3.85 (H, t, J=11 Hz), 4.30 (H, m), 4.55 (H, m), 5.08 (H, m) 7.3-7.5(6H, m) 7.6-7.8 (4H, m).

(h) 6(R)-[2-[8(S)-(2,2-Dimethylbutyryloxy)-2(S)-methyl-6(S)-hydroxymethyl-1,2, 3,4,4a(S),5,6,7,8,8a (S)-decahydronaphthyl-l(S)]ethyl]-4(R)-hydroxy-3,4,5,6- tetrahydro-2H-pyran-2one. (2h)

Tetra-n-butylammonium fluoride solution (1 ml, 1 M,1 mmol) was added to a stirred mixture of compound 2g (55 mg, 0.0695 mmol) and acetic acid (0.12 ml, 2.10 mmol) in tetrahydrofuran (1.2 ml). The resulting mixture was stirred at room temperature for 36 hours. The reaction mixture was heated at

reflux for 4.5 hours, cooled to room temperature and poured into cold water and extracted with diethyl ether. The ethereal extract was washed with 5% NaHCO.sub.3, dried, filtered, and concentrated in vacuo to yield a residue which was purified by flash chromatography on silica gel. Elution of the column with methylene chloride:acetone (10:1; v:v) removed the impurities. Further elution with methylene chloride:acetone:isopropanol (100:10:5; v:v:v) afforded the desired compound as a gummy oil ; 1.sub.H nmr (CDCl.sub.3) .delta. 0.85 (3H, d, J=7 Hz), 0.87 (3H, t, J=7 Hz) 1.16 (3H, s), 1.17 (3H, s), 2.62 (H, m of d, J=18 Hz), 2.73 (H, d of d, J=18, 5 Hz), 3.0 (H, bs), 3.57 (H, d of d, J=11,6 Hz), 3.80 (H, t, J=11 Hz) 4.34 (H, m), 4.60 (H, m) 5.20 (H, m).

Anal Calc'd for C.sub.25 H.sub.42 O.sub.6 : C, 68.46; H, 9.65. Found: C, 68.35; H, 9.85.

EXAMPLE 3

Preparation of 6(R)-[2-[8(S) (2,2-dimethylbutyryloxy)- 2-(S)-methyl-6(S)-(1 hydroxyethyl)-1,2,3,4,4a (S),5,6,7,8,8a(S)-decahydronaphthyl-1(S)]ethyl]-4(R)-hydroxy-3,4,5,6-tetrahydro-2H-pyran-2-one

(a) 6(R)-[2-[8(S)-Nitrosyloxy-2(S),6(S)-dimethyl-1,2,3,4,4a(S),5,6,7,8,8a(S)-d ecahydronaphthyl-1(S)] ethyl]-4(R)-(tert-butyldimethylsilyloxy)-3,4,5,6-tetr ahydro-2H-pyran-2-one (3a)

A stream of nitrosyl chloride gas was passed into a stirred solution of 6(R)-[2-[8(S)-hydroxy-2(S)-6(S)-dimethyl-1,2,3,4,4a(S),5,6,7,8,8a(S)-decah ydronaphthyl-1(S)]ethyl]-4(R)-(tert-butyldimethylsilyloxy)-3,4,5,6-tetrahyd ro-2H-pyran-2-one (800 mg, 1.82 mmol) in pyridine (14 ml) at 0.degree. C. until the solution was saturated (brownish fumes filled the reaction flask). The resulting mixture was stirred at 0.degree. C. for another 10 minutes, poured into cold water and extracted with diethyl ether. The extract was washed successively with dilute HCl, water and 5% NaHCO.sub.3, dried (MgSO.sub.4), filtered and concentrated in vacuo to afford the title compound as a white solid; mp 92.degree.-4.degree. C.; 1.sub.H nmr (CDCl.sub.3) .delta. 0.86 (3H, d, J=7 Hz), 0.89 (9H, s), 0.99 (3H, d, J=7 Hz), 2.55 (H, m of d, J=18 Hz), 2.60 (H, d of d, J=18,4 Hz), 4.28 (H, m), 4.53 (H, m), 5.84 (H, m).

Anal Calc'd for C.sub.25 H.sub.45 NO.sub.5 Si: C, 64.20; H, 9.70; N, 3.00. Found: C, 64.09; H, 10.00; N, 3.06.

(b) 6(R)-[2-[8(S)-Hydroxy-2(S)-methyl-6(S)-nitrosylmethyl-1,2,3,4,4a(S),5,6,7, 8,8a(S)-decahydronaphthyl-1(S)]ethyl]-4(R)-(tert-butyldimethylsilyloxy)-3,4 ,5,6-tetrahydro-2H-pyran-2-one (3b)

Nitrogen gas was passed through a solution of compound 3a (870 mg, 1.82 mmol) in benzene (320 ml) for 25 minutes. This solution was irradiated under N.sub.2 with a 450 watt Hanovia medium pressure mercury lamp (pyrex filter) for 40 minutes at room temperature. The reaction mixture was then concentrated in vacuo and the residue applied to a silica gel column. Elution of the column with methylene chloride:acetone (50:1; v:v) followed by elution with methylene chloride:acetone: isopropanol (100:10:2; v:v:v) yielded the desired product as a foamy oil; 1.sub.H nmr (CDCl.sub.3) .delta. 0.83 (3H, d, J=7 Hz), 0.88 (9H, s) 4.10 (H, bs), 4.29 (H, m), 4.64 (2H, d, J=8 Hz), 4.67 (H, m).

(c) 6(R)-[2-[8(S)-Hydroxy-2(S)-methyl-6(S)-hydroxyiminomethyl-1,2,3,4,4a(S),5, 6,7,8,8a(S) decahydronaphthyl-1(S)]ethyl]-4(R)-(tert-butyl-dimethylsilyloxy)-3,4,5,6-t etrahydro-2H-pyran-2 one (3c)

Compound 3b (288 mg, 0.616 mmol) was dissolved in isopropanol (15 ml) and heated at reflux for 2 hours. After cooling the reaction mixture was concentrated in vacuo to leave a residue which afforded

the title compound as a gummy oil; 1.sub.H nmr (CDCl.sub.3) .delta. 0.86 (3H, d, J=7 Hz), 0.90 (9H, s) 2.33 (H, d, J=14 Hz), 2.78 (H, m), 4.11 (H, m), 4,32 (H, m), 4.66 (H, m), 7,50 (H, d, J=6 Hz).

(d) 6(R)-[2-[8-Hydroxy-2(S)-methyl-6(S)-formyl-1,2,3,4,4a(S),5,6,7,8,8a(S)-dec ahydronaphthyl-1(S)]-ethyl]-4(R)-(tert-butyldimethylsilyloxy)-3,4,5,6-tetra hydro-2H-pyran-2-one (3d)

Sodium nitrite (477 mg 6.83 mmol) was added at 0.degree. C. in one portion to a stirred solution of compound 3c (324 mg 0.683 mmol) in acetic acid (14 ml) and water (7 ml). The resulting mixture was stirred at 0.degree. C. for 10 minutes, warmed to room temperature and stirred for 2.5 hours. The mixture was then diluted with water and extracted with diethyl ether. This ethereal extract was washed with water, 5% NaHCO.sub.3 (twice), dried and filtered. Evaporation of the filtrate in vacuo afforded a brownish oily residue whose nmr spectrum is consistent with the structure for compound 2d; 1.sub.H nmr CDCl.sub.3) .delta. 0.80 (3H, d, J=7 Hz), 0.88 (9H, s), 4,30 (H, m) 4.55 (2H, m).

(e) 6(R)-[2-[8(S)-Hydroxy-2(S)-methyl-6(S)-hydroxymethyl-1,2,3,4,4a(S),5,6,7,8 ,8a(S)-decahydronaphthyl-1(S)]ethyl]-4(R)-(tert-butyldimethylsilyloxy)-3,4, 5,6-tetrahydro-2H-pyran-2-one (3e)

Powdered sodium borohydride (40 mg, 1.05 mmol) was added at 0.degree. C. to a stirred solution of compound 3d (296 mg, 0.651 mmol) in 95% ethanol (15 ml) in one portion. The resulting mixture was stirred at 0.degree. C. for 0.5 hours, then slowly treated with a solution of aqueous (NH.sub.4).sub.2 SO.sub.4 (0.7 g in 15 ml of 2 H.sub.2 O). The resulting mixture was stirred at O.degree. C. for 0.5 hours, diluted with water (60 ml) and extracted with diethyl ether. This extract was washed with water, 5% NaHCO.sub.3, dried, filtered and evaporated to give a crude sample which was purified by flash chromatography. Elution of the column with methylene chloride:acetone:isopropanol (100:10:2; v:v:v) afforded the desired product as a white solid; mp 124.degree.-7.degree. C.; 1.sub.H nmr (CDCl.sub.3) .delta. 0.83 (3H, d, J=7 Hz), 0.90 (9H, s), 3.73 (H, d of d, J=11,6 Hz), 3.79 (H, d of d, J=11,6 Hz), 4.10 (H, bs) 4.31 (H, m), 4.70 (H, m).

Anal Calc'd for C.sub.25 H.sub.46 O.sub.5 Si C, 66.03; H, 10.20. Found: C, 66.07; H, 10.38.

(f) 6(R)-[2-[8(S)-hydroxy-2(S)-methyl-6(S)-benzyloxymethoxymethyl-1,2,3,4,4a(S),5,6,7,8,8a(S)-decahydronaphthyl-1(S)]-ethyl]-4(R)-tert-butyldimethylsilyl oxy)-3,4,5,6-tetrahydro-2H-pyran-2-one (3f)

To a stirred solution of compound 3e (9.7 g, 21.3 mmol) and diisopropylethylamine (10 mL, 57.4 mmol) in CH.sub.2 Cl.sub.2 (25 mL) cooled to 0.degree. C. was added dropwise a solution of benzyl chloromethyl ether (3.76 g, 24 mmol) in CH.sub.2 Cl.sub.2 (10 mL). The resulting mixture was stirred at 0.degree. C. for 10 minutes, allowed to warm to room temperature, stirred at room temperature for 22 hours and then poured into ice water. The heterogeneous mixture was extracted with diethyl ether. The organic phase was separated, washed successively with dilute HCl, water, aqueous NaHCO.sub.3 and water, dried (Na.sub.2 SO.sub.4), filtered and evaporated in vacuo to afford a residue which was purified by flash chromatography on silica gel. Elution with CH.sub.2 Cl.sub.2 acetone (50:1; v:v) removed the impurities. Continued elution with CH.sub.2 Cl.sub.2 acetone (20:1; V:V) provided the title compound as a viscous oil; 1.sub.H nmr (CDCl.sub.3) .delta. 0.82 (3H, d, J=7 Hz), 0.88 (9H, s), 2.6 (2H, m), 2.70 (H, d, J=6 Hz), 3.75 (2H, m), 4.0 (H, m), 4.28 (H, m), 4.60 (H, d, J=12 Hz), 4.62 (H, d, J=12 Hz), 4.66 (H, m), 4.78 (H, d, J=6 Hz), 4.81 (H, d, J=6 Hz), 7.3 (5H, m).

(g) 6(R)-[2-[8(S)-(2,2-Dimethylbutyryloxy)-2(S)-methyl-6(S)-benzyloxymethoxyme thyl-1,2,3,4,4a (S),5,6,7,8,8a(S)-decahydronaphthyl-1(S)]ethyl]-4(R)-(tert-b utyldimethylsilyloxy)-3,4,5,6-tetrahydro-2H-pyran-2-one (3g)

Powdered lithium bromide (6.4 g, 74 mmol) was added under N.sub.2 to a stirred mixture of 2,2-dimethylbutyryl chloride (4.97 g, 37 mmol) in pyridine (100 mL) and the resulting mixture was stirred and warmed to 40.degree. C. until a clear solution was obtained. To the resulting solution was added 4-dimethylaminopyridine (0.3 g, 2.45 mmol) and a solution of 3f (7.25 g, 13 mmol) in pyridine (30 mL). The resulting mixture was stirred and heated at 90.degree. C. for 3.5 hours, cooled to room temperature, poured into ice water and extracted with diethyl ether. The organic phase was separated, washed with dilute HCl, aqueous NaHCO.sub.3 and saturated brine, dried (Na.sub.2 SO.sub.4), filtered and evaporated in vacuo to give an oily residue which was purified by flash chromatography on silica gel. Elution with CH.sub.2 Cl.sub.2 -acetone (50:1; v:v) afforded the title compound as a viscous oil; 1.sub.H nmr (CDCl.sub.3) .delta. 0.82 (3H, d, J=7HZ), 0.83 (3H, t, J=7 Hz), 0 88 (9H, s), 1.14 (3H, s), 1.15 (3H, s), 2.67 (2H, m), 3.39 (H, d of d, J=10, 6 Hz), 3.86 (H, t, J=10 Hz), 4.27 (H, m), 4.54 (H, d, J=16 Hz), 4.61 (H, d, J=16 Hz), 4.74 (2H, s), 5.13 (H, m), 7.32 (5H, m).

(h) 6(R)-[2-[8(S)-(2,2-Dimethylbutyryloxy)-2(S)-methyl-6-(S)-hydroxymethyl-1,2 ,3,4,4a(S),5,6,7,8,8a (S)-decahydronaphthyl-(S)]ethyl]-4(R)-(tert-butyldimethylsilyloxy)-3,4,5,6 -tetrahydro-2H-pyran-2-one (3h)

A mixture of compound 3g (6.1 g, 8.85 mmol), 10% Pd/C (0.5 g) and acetic acid (3 drops) in isopropanol (200 mL) was hydrogenated in a Paar apparatus for 4 hours. The resulting mixture was treated with powdered NaHCO.sub.3 (1 g), stirred for 15 minutes and filtered. The filtrate was evaporated in vacuo to provide a residue which was dissolved in toluene (100 mL). The resulting solution was evaporated in vacuo to provide a residue which again was dissolved in toluene (100 mL). Evaporation of this solution in vacuo gave a residue which crystallized from diethyl ether hexane to provide the title compound as a colorless solid, mp 70.degree.-71.degree. C.; 'H nmr (CDCl.sub.3) .delta. 0.82 (3H, d, J=7 Hz), 0.83 (3H, t, J=7 Hz), 0.87 (9H, s), 1.15 (3H, s), 1.16 (3H, s), 2.66 (2H, m), 3.55 (H, m), 3.78 (H, m), 4.28 (H, m), 4.65 (H, m), 5.14 (H, m).

Anal. Cal'd for C31H56O6Si: C, 67.34; H, 10.21. Found: C, 67.21; H, 10.35.

6(R)-[2-[(S)-(2,2-Dimethylbutyryloxy)-2(S)-methyl-6(S)-formyl-1,2,3,4,4a(S) ,5,6,7,8,8a(S)-decahydronaphthyl-1(S)]-ethyl]-4(R)-(tert-butyldimethylsilyl oxy)-3,4,5,6-tetrahydro-2H-pyran-2-one (3i)

To a stirred solution of oxalyl chloride (152 mg, 1.2 mmol) in CH.sub.2 Cl.sub.2 (10 mL) cooled at -78.degree. C. was added dimethylsulfoxide 156 mg, 2 mmol) via syringe under N.sub.2. The resulting mixture was stirred at -78.degree. C. for 15 minutes and treated with a solution of compound 3h (383 mg, 0.693 mmol) in CH.sub.2 Cl.sub.2 (5 mL) added dropwise. The resulting mixture was stirred at -78.degree. C., for 30 minutes, treated with triethylamine (253 mg, 2.5 mmol), stirred for an additional 10 minutes at -78.degree. C. warmed to room temperature, poured into ice water and extracted with diethyl ether. The organic extract was washed with aqueous NaHCO.sub.3 and water, dried (Na.sub.2 SO.sub.4), filtered and evaporated in vacuo to provide the title compound as a pale yellow oil; 1.sub.H nmr (CDCl.sub.3) .delta. 0.83 (3H, d, J=7 Hz), 0.83 (3H, t, J=7 Hz), 0.89 (9H, s), 1.10 (3H, s), 1.12 (3H, s), 2.58 (2H, m), 4.28 (H, m), 4.55 (H, m), 5.20 (H, m), 9.63 (H, s).

(j) 6(R)-[2-[8(S)-(2,2-Dimethylbutyryloxy)-2(S)-methyl-6(S)-(1-hydroxyethyl)-1 ,2,3,4,4a(S),5,6,7,8,8a (S)-decahydronaphthyl-1(S)]-ethyl]-4(R)-(tert-butyld imethylsilyloxy)-3,4,5,6-tetrahydro-2H-pyran-2-one (3j)

A solution of methylmagnesium bromide (3.0M in diethyl ether, 0.50 mL, 1.5 mmol) was added dropwise to a stirred solution of compound 3i (700 mg, 1.27 mmol) dissolved in dry diethyl ether (20

mL) at -78.degree. C. under an argon atmosphere. The cooling bath was removed and the reaction mixture was stirred with gradual warming to room temperature over about a 2 hour period before quenching with a saturated brine solution (10 mL). The reaction mixture was distributed between diethyl ether (100 mL) and water (50 mL). The diethyl ether layer was separated, dried, filtered and evaporated to leave crude product which was purified by flash chromatography on a silica gel column. Elution of the column with chloroform:acetone (40:1/v:v) gave the two diastereomeric alcohols as clear colorless glasses.

Isomer A: R.sub.f =0.17, diagnostic nmr peaks (CDCl.sub.3) .delta. 4.02 (H, m), 4.27 (H, m), 4.54 (H, m), 5.12 (H, m).

Isomer B: R.sub.f =0.07, diagnostic nmr peaks (CDCl.sub.3) .delta. 3.98 (H, m), 4.27 (H, m), 4.56 (H, m), 5.16 (H, m).

(k) 6(R)-[2-[8(S)-(2,2-dimethylbutyryloxy)-2(S)-methyl-6(S)-(1 hydroxyethyl)-1,2,3,4,4a,(S),5,6,7,8,8a (R)-decahydronaphthyl-1(S)]ethyl]-4 (R)-hydroxy-3,4,5,6-tetrahydro-2H-pyran-2-one (Isomer A)

n-Tetrabutylammonium fluoride solution (1M in THF, 1.65 mL, 1.65 mmol) was added to a stirred solution of compound 3j isomer A (180 mg, 310 .mu.mol) and acetic acid (180 .mu.L) in tetrahydrofuran (3 mL). The resulting solution was stirred at room temperature for 18 hours. Thin layer chromatography now showed only a trace of silyl ether and was thus diluted with water (30 mL) and the crude product was extracted into diethyl ether (100 mL). The etherial extract was washed with 0.1N hydrochloric acid (100 mL), water (2.times.50 mL), saturated sodium bicarbonate solution (50 mL), dried, filtered, and evaporated to yield the crude alcohol which was purified by flash chromatography on silica gel. Elution of the column with methylene chloride:acetone (6:1/v:v) gave the desired diol as a clear colorless glass: R.sub.f =0.46 chloroform:acetone (4:1/v:v), diagnostic nmr peaks (CDCl.sub.3) 6 2.6 (H, md, J=18 Hz), 2.73 (H, dd, J=5, 18 Hz), 4.03 (H, m), 4.35 (H,m), 4.56 (H,m), 5.15 (H,m).

Anal Calc'd for C.sub.26 H.sub.44 O.sub.6 : C, 68,99; H, 9.80. Found: C, 69.07; H, 9.82.

(l) 6(R)-[2-[8(S)-(2,2-dimethylbutyryloxy)-2(S)-methyl-6(S)-(1-hydroxyethyl)-1 ,2,3,4,4a,(S),5,6,7,8,8a (R)-decahydronaphthyl-1(S)]ethyl]-4(R)-hydroxy-3,4, 5,6-tetrahydro-2H-pyran 2-one (Isomer B)

Aqueous hydrofluoric acid (49%, 0.42 mL) was added dropwise to a stirred solution of compound 3j isomer B (200 mg, 0.34 mmol) in acetonitrile (8 mL) at about 10.degree. C. The cooling bath was removed and the clear colorless solution was stirred at room temperature for 11/4 hour. The reaction mixture was distributed between diethyl ether (100 mL) and saturated sodium bicarbonate solution (50 mL). The ethereal layer was dried, filtered, and evaporated to provide crude diol which was purified by flash chromatography on silica gel. Elution of the column with methylene chloride:acetone (6:1/v:v) gave the desired diol as a clear colorless glass: R.sub.f =0.31 chloroform:acetone (4:1/v:v), diagnostic nmr peaks (CDCl.sub.3) .delta. 2.6 (H, md, J=18 Hz), 2.73 (H, dd, J=5,18 Hz), 3.98 (H, m), 4.14 (H, m), 4.56 (H,m), 5.18 (H, m). MS (FAB)m/z 453 (MH.sup.+).

Anal Calc'd for C.sub.26 H.sub.44 O.sub.6 : C, 68.99; H, 9.80. Found: C, 68.96; H, 10.04.

EXAMPLE 4

(j) 6(R)-[2-[8(S)-(2,2-Dimethylbutyryloxy)-2(S)-methyl-6(S)-(.alpha.-hydroxybe nzyl)-1,2,3,4,4a (S),5,6,7,8,8a(S)-decahydronaphthyl-1(S)]ethyl]-4(R)-(tert butyldimethylsilyloxy)-3,4,5,6-tetrahydro-2H-pyran 2 one (4j)

Utilizing the general method described in Example 3 step j except that the methylmagnesium bromide was replaced by phenylmagnesium chloride the above titled compound was obtained as a single diastereomer.

(k) 6(R) [2-[8(S)-(2,2-Dimethylbutyryloxy)-2(S)-methyl-6(S)-(.alpha.-hydroxybenzyl- 1,2,3,4,4a (S),5 ,6,7,8,8a-(S)-decahydronaphthyl-1(S)]ethyl]-4(R) hydroxy-3,4,5,6 tetrahydro-2H-pyran 2 one (4k)

Utilizing the general method described in Example 3 step 1 except that 1; isomer A was replaced by 4j, the above titled compound was obtained as a colorless solid following recrystallization from acetonitrile water, mp 196.degree.-196.5.degree. C., diagnostic nmr peaks (CDCl.sub.3) .delta. 2.64 (H, md, J=18 Hz), 2.74 (H, dd, J=5, 18 Hz), 4.35 (H, m) 4.59 (H, m), 4.88 (H, dd, J=3, 10.8 Hz), 5.29 (H, d, J=3 Hz).

Anal. Calc'd for C.sub.31 H.sub.46 O.sub.6 : C, 72.34; H, 9.01 Found: C, 72.29; H, 9.29.

EXAMPLE 5

Preparation of 6(R)-[2-[8(S)-(Cyclohexylcarbonyloxy)-6(S)-hydroxymethyl-2(S)-methyl-1,2,3 ,4,4a (S),5,6,7,8,8a(S)-decahydronaphthyl-1(S)]ethyl]-4(R)-hydroxy-3,4,5,6-t etrahydro-2H-pyran-2-one

(a) 6(R)-[2-[8(S)-Cyclohexylcarbonyloxy)-6(S)-(tert-butyldiphenylsilyloxymethy l)-2(S)-methyl-1,2,3,4,4a(S),5,6,7,8,8a(S)-decahydronaphthyl-1(S)]ethyl]-4(R)-(tert butyldimethylsilyloxy)-3,4,5,6-tetrahydro-2H-pyran-2-one (5a)

A solution of cyclohexylcarbonyl chloride (73 mg, 0.5 mmol) in pyridine (2 ml) was added to a stirred mixture of 6(R)-[2-[8(S)-hydroxy-2(S)-methyl-6(S)-(tert-butyldiphenylsilyloxymethyl)- 1,2,3,4,4a (S),5,6,7,8,8a(S)-decahydronaphthyl-1(S)]ethyl]-4(R)-(tert-butyld imethylsilyloxy)-3,4,5,6-tetrahydro-2H-pyran-2-one (116 mg, 0.167 mmol), the compound 2f, and 4 (dimethylamino)pyridine (24 mg, 0.2 mmol) in pyridine (2 ml). The resulting mixture was stirred at room temperature under N.sub.2 for 3 hours and then heated at 65.degree. C. for 1.5 hours. After cooling, the reaction mixture was poured into cold water and extracted with diethyl ether. The ethereal extract was washed successively with dilute hydrochloric acid, water and 5% NaHCO.sub.3. After drying, it was filtered and evaporated in vacuo to leave a residue which was purified by flash chromatography. Elution of the column with methylene chloride:acetone (100:1; V:V) yielded the desired compound as a colorless gummy oil; 1.sub.H nmr (CDCl.sub.3) .delta. 0.83 (3H, d, J=7 Hz), 0.90 (9H, s), 1.08 (9H, s), 3.54 (H, d of d, J=11, 6 Hz), 3.83 (H, t, J=11 Hz), 4.28 (H, m), 4.56 (H, m), 5.04 (H, m), 7.32 7.5 (6H, m), 7.6 7.8 (4H, m).

(b) 6(R)-[2-[8(S)-(Cyclohexylcarbonyloxy) 6(S)-hydroxymethyl-2(S)-methyl-1,2,3,4,4a(S),5,6,7,8,8a (S)-decahydronaphth yl-1(S)]ethyl]-4(R)-hydroxy-3,4,5,6-tetrahydro-2H-pyran-2 one (5b)

By following the general procedure of Example 2, Step (h), but using compound 5a in place of compound 2h, there was obtained the desired product as a colorless, gummy oil; 1.sub.H nmr (CDCl.sub.3) .delta. 0.86 (3H, d, J=7 Hz), 2.30 (H, m), 2.63 (H, m of d, J=18 Hz), 2.76 (H of d, J=18, 5 Hz), 3 58 (H, d of d, J=11, 6 Hz), 3.81 (H, t, J=11 Hz), 4 37 (H, m), 4.60 (H, m), 5.18 (H, m).

Anal Calc'd for C.sub.26 H.sub.42 O.sub.6 .multidot.0.4H.sub.2 O: C, 68.21; H, 9.42. Found: C, 68.15; H, 9.53.

EXAMPLE 6

Preparation of 6(R)-[2-[8(S)-(2,2-Dimethylbutyryloxy)-6(R)-hydroxymethyl-2(S)methyl-1,2,3 ,4,6,7,8,8a(R)-octahydronaphthyl-1(S)]ethyl]-4(R)-hydroxy-3,4,5,6-tetrahydr o-2H-pyran-2-one

(a) 6(R)-[2-[8(S)-Hydroxy-2(S),6(R)-dimethyl-1,2,3,4,6,7,8,8a(R)-octahydronaph thyl-1(S)]ethyl]-4(R)-(tert-butyldimethylsilyloxy)-3,4,5,6-tetrahydro-2H-py ran-2-one

A solution (200 ml) of 50% toluene in absolute ethanol was deoxygenated by bubbling N.sub.2 through it for 15 minutes. Wilkinson's catalyst (2 g) was added to the solution and the mixture reduced on the Paar hydrogenation apparatus at 50 psi H.sub.2 for 90 minutes. 6(R)-[2-[8(S)-Hydroxy-2(S),6(R)-dimethyl-1,2,6,7,8,8a-(R)-hexahydronaphthy l-1(S)]ethyl]-4(R)-(tert-butyldimethylsilyloxy)-3,4,5,6-tetrahydro-2H-pyran -2-one (4.0 g, 9.0 mmol.) was added and the solution hydrogenated at 58 psi H.sub.2 for two days. The solvent was removed in vacuo and the residue stirred with diethyl ether (500 ml) for 15 minutes and then filtered. The filtrate was evaporated in vacuo to give a brown solid which was dissolved in toluene (200 ml) containing thiourea (2.6 The mixture was heated at 80.degree. C. for 2 hours and then cooled to 0.degree. C. and filtered. The filtrate was evaporated in vacuo and the solid residue chromatographed on a 7.times.18 cm column of silica gel. The column was eluted with 20% ethyl acetate in hexane and 25 ml fractions were collected. Fractions 54-90 were combined and evaporated in vacuo to yield the title compound as a colorless solid. Crystallization of the solid from aqueous CH.sub.3 CN provided an analytical sample as colorless needles, mp 145.degree.-6.degree. C.; 1.sub.H nmr (CDCl.sub.3) .delta. 0.070 (3H, s), 0.077 (3H, s), 0.88 (9H, s), 0.90 (3H, d, J=7 Hz), 1,17 (3H, d, J =7 Hz), 2,58 (2H, m), 4,16 (H, m), 4.28 (H, m), 4.66 (H, m), 5.41 (H, m).

Anal Calc'd for C.sub.25 H.sub.44 O.sub.45 : C, 68.76, H, 10.50. Found: C, 68.72; H, 10.32.

(b) 6(R)-[2-[8(S)-(2,2-Dimethylbutyryloxy)-6(R)-hydroxymethyl-2(S)-methyl-1,2, 3,4,6,7,8,8a(R)-octahydronaphthyl-1(S)]ethyl]-4(R)-hydroxy-3,4,5,6-tetrahyd ro-2H-pyran-2-one

By substituting an equimolar amount of the title compound in Step (a) of this example for 6(R)-[2-[8(S)-hydroxy-2(S),6(S)-dimethyl-1,2,3,4,4a-5,6,7,8,8a(S)-decahydr onaphthyl-1(S)]ethyl]-4(R)-(tert-butyldimethylsilyloxy)-3,4,5,6-tetrahydro- 2H-pyran-2-one in Step (a) of Example 2 and then following the general procedures of Steps (a) through (h) of Example 2, there was obtained a corresponding amount of the title compound as an amorphorus solid; 1.sub.H nmr (CDCl.sub.3) .delta. 0.85 (3H, t, J=Hz), 0.90 (3H, d, J=7 Hz), 1,14 3H, s), 1,16 (3H, s), 3.54 (H, m), 3.65 (H, m), 4.37 (H, m), 4.59 (H, m), 5.35 (H, m), 5.47 (H, m).

Anal Calc'd for C.sub.25 H.sub.40 O.sub.6 .multidot.0.5H.sub.2 O: C, 67.38; H, 9.57. Found: C, 67.66; H, 9.28.

EXAMPLE 7

Preparation of 6(R)-[2-[8(S)-(2,2-Dimethylbutyryloxy)-2(S)-methyl-6(S)-carboxy-1,2,3,4,4a (S),5,6,7,8,8a(S)-decahydronaphthyl-1(S)]ethyl]4(R)-hydroxy 3,4,5,6-tetrahydro-2H-pyran-2-one (a)

6(R)-[2-[8(S)-2,2-Dimethylbutryloyxy)-2(S)-methyl-6(S)-formyl-1,2,3,4,4a(S) ,5,6,7,8,8a(S)-decahydronaphthyl-1(S)]ethyl]-4(R)-hydroxy 3,4,5,6-tetrahydro-2H-pyran 2-one (7a)

A mixture of compound 2h (100 mg, 0.228 mmol), tris(triphenylphosphine) ruthenium (II) chloride (120 mg, 0.125 mmol) and sodium carbonate (40 mg) in benzene (7 ml) and methylene chloride (2 ml) was stirred at ambient temperature under N.sub.2 for 24 hours. The reaction mixture was diluted with diethyl ether (10 ml) and filtered through diatomaceous earth and silica gel which was subsequently washed with methylene chloride. The combined filtrate and washings were concentrated in vacuo to yield a crude residue. The residue was purified by flash chromatography on silica gel eluted with methylene chloride:acetone:isopropanol (100:10:2; V:V:V) to afford the desired product as a gummy oil; 1.sub.H

nmr (CDCl.sub.3) .delta. 0.82 (3H, d, J=7 Hz), 0.83 (3H, t, J=7 Hz), 1.10 (3H,s), 1.12 (3H,s), 2.60 (H, m of d, J=18 Hz), 2.73 (H, d of d, J=18,5 Hz), 4.37 (H,m), 4.57 (H,m), 5.23 (H,m), 9.64 (H, s)

(b) 6(R)-[2-[8(S)-(2,2-Dimethylbutyryloxy)-2(S)-methyl-6(S)-carboxy-1,2,3,4,4a (S)5,6,7,8,8a(S)-decahydronaphthyl-1(S)]ethyl]4(R)-hydroxy 3,4,5,6-tetrahydro- 2H-pyran-2-one (7b)

To a stirred mixture of compound 7a (14 mg, 0.032 mmol) and sulfamic acid (4.4 mg, 0.045 mmol) in THF (1.5 ml) and water (0.5 ml) was added solid sodium chlorite (80% active, 5.6 mg, 0.05 mmol). The reaction mixture was stirred at ambient temperature for 45 minutes, poured into cold water (15 ml) and extracted with diethyl ether and methylene chloride. The organic phase was separated, dried (MgSO.sub.4) filtered and evaporated in vacuo to give a crude residue. The residue was purified by flash chromatography on silica gel eluted with methylene chloride:acetone:isopropanol (100:10:5; v:v:v) to afford the desired product as a gummy oil; 1.sub.H nmr (CDCl.sub.3) .delta. 0.83 (3H, d, J=7 Hz), 0.83 (3H, t, J=7 Hz), 1.08 (3H, s), 1.09 (3H, s), 2.14 (H, m of d, J=13 Hz), 2.73 (H, d of d, J=18,5 Hz), 4.36 (H, m), 4.57 (H, m), 5.19 (H, m).

EXAMPLE 8

Preparation of 6(R)-[2-[8(S)-(2,2-Dimethylbutyryloxy)-2(S)-methyl-6(S)-methoxycarbonyl-1, 2,3,4,4a (S)5,6,7,8,8a(S)-decahydronaphthyl-1(S)]ethyl]4(R)-hydroxy-3,4,5,6- tetrahydro-2H-pyran-2-one

To a solution of compound 7b (9.6 mg, 0.021 mmol) in isopropanol (2 ml) at ambient temperature was added a solution of trimethylsilyl-diazomethane 10% in hexane, 0.3 ml. The reaction mixture was stirred at ambient temperature for 18 hours and then concentrated in vacuo to give a crude residue. The residue was purified by flash chromatography on silica gel eluted with methylene chloride:acetone:isopropanol 100:10:2; v:v:v) to afford the desired product as a gummy oil; 1.sub.H nmr (CDCl.sub.3) .delta. 0.83 (3H, d, J=7 Hz), 0.83 (3H, t, J=7 Hz), 1.09 (3H, s), 1.12 (3H,3), 1.52 (2H, t, J=7 Hz), 2.16 (H, m of d, J=13 Hz), 2.60 (H, m of d, J=18 Hz), 2.74 (H, d of d, J=18,5 Hz), 3.66 (3H,s), 4.37 (H, m), 4.57 (H, m), 5.18 (H, m).

EXAMPLE 9

Preparation of 6(R)-[2-[8(S)-(2,2-Dimethylbutyryloxy)-6(R)-(2,2-dimethylbutyryloxymethyl) -2(S)-methyl-1,2,3,4,6,7,8,8a(R)-octahydronaphthyl-1(S)]-ethyl]-4(R)-hydrox y-3,4,5,6-tetrahydro-2H-pyran-2-one

To a solution of tetra-n-butylammonium fluoride (211 .mu.l, 1M in tetrahydrofuran, 0.21 mmol), acetic acid (17 mg, 0.28 mmol) and tetrahydrofuran (5 ml) was added 6(R)-[2-[8(S)-(2,2-dimethylbutyryloxy)-6(R)-(2,2-dimethylbutyryloxymethyl) -2(S)-methyl-1,2,3,4,6,7,8,8a(R)-octahydronaphthyl-1(S)]-ethyl]-4(R)-(tert- butyldimethylsilyloxy)-3,4,5,6-tetra-hydro-2H-pyran-2-one which was isolated from the reaction of 2,2-dimethylbutyryl chloride and 6(R)-2-[8(S)-hydroxy-6(R)-(tert-butyldimethylsilyloxymethyl)-2(S)-methyl-1 ,2,3,4,6,7,8,8a(R)-octahydronaphthyl-1(S)]ethyl]4(R)-(tert-butyldimethylsil yloxy)-2,3,5,6-tetra-hydro-2H-pyran-2-one according to the general procedure of Example 2, Step (g). The reaction mixture was stirred at ambient temperature for 18 hours and then evaporated in vacuo to give a crude residue. The residue was partitioned between diethyl ether (50 ml) and water (10 ml). The aqueous phase was washed with diethyl ether (2.times.50 ml). The combined organic phase and the washings were washed with saturated sodium bicarbonate (5 ml) and brine (2.times.25 ml), dried (MgSO.sub.4) and evaporated in vacuo to yield a gummy residue. The residue was purified by flash chromatography on silica gel eluted with 10 percent acetone in methylene chloride (150 ml) and then 20 percent acetone in methylene chloride to afford the desired product. This product was further purified by preparative high pressure liquid chromatography and after trituration with

hexane gave a crystalline product; mp 119.degree.-121.degree. C.; 1.sub.H nmr (CDCl.sub.3) .delta. 0.84 (6H, m), 0.90 (3H, d, J=7 Hz), 1.14 (12H, s), 3,83 (1.sub.H d of d, J=10,9 Hz), 4.19 (H, d of d, J=10,9 Hz), 4.37 (H, m), 4.59 (H, m), 5.36 (H, m), 5.40 (H, m), FAB MS 535 (M+H), 557 (M+Na).

EXAMPLE 10

Preparation of 6(R)-[2-[8(S)-(2,2-Dimethylbutyryloxy)-6(S)-hydroxymethyl-2(S)-methyl-1,2, 6,7,8,8a (R)-hexahydronaphthyl-1(S)]ethyl]-4(R)-hydroxy-3,4,5,6-tetrahydro-2 H-pyran-2-one

To a stirred solution of 6(R)-[2-[8(S)-(2,2-dimethylbutylbutyryloxy)-6(S)-carboxy-2(S)-methyl-1,2,6 ,7,8,8a(R)-hexahydronaphthyl-1(S)]ethyl]-4(R)-hydroxy-3,4,5,6-tetrahydro 2H-pyran 2-one (102 mg, 0.23 mmol) in 4 .ANG. sieve-dried CH.sub.2 Cl.sub.2 (2.3 mL) was added triethylamine (32 .mu.l, 0.23 mmol). The resulting mixture was cooled to -70.degree. C. and isobutyl chloroformate (30 .mu.l, 0.23 mmol) was added over a 30-second period with stirring. After stirring for 30 minutes at -70.degree. C., the mixture was allowed to warm to 0.degree. C. over a 20 minute period. The resulting solution was added over a 30 second period to a freshly prepared solution of NaBH.sub.4 (8.8 mg, 0.23 mmol) in EtOH (2 ml) with stirring at 0.degree. C. After 10 minutes, the cold mixture was partitioned between EtOAc (20 mL) and 0.1N HCl. The organic phase was separated, washed with water (2.times.5 mL) and saturated brine (5 mL), dried (Na.sub.2 SO.sub.4), filtered and evaporated viscous oil (95 mg). Chromatography of this oil on silica gel using 0 10% CH.sub.30 H in CHCl.sub.3 as eluant afforded the title compound which was identical by comparative tlc and 1.sub.H nmr spectral analysis to an authentic sample isolated from a microbiological fermentation broth of the sodium salt of 7-[1,2,6,7,8,8a(R)-hexahydro-2(S),6(R)-dimethyl-8(S)-(2,2-dimethylbutyrylo xy)-1(S)naphthyl]-3(R),5(R)-dihydroxyheptanoic acid.

EXAMPLE 11

Preparation of 6(R)-[2-[8(S)-(2,2-Dimethylbutyryloxy)-6(R)-hydroxymethyl-2(S)-methyl-1,2, 6,7,8,8a (R)-hexahydronaphthyl-1(S)]ethyl]-4(R)-hydroxy-3,4,5,6-tetrahydro-2 H-pyran-2-one

By substituting an equimolar amount of the 6(R)-carboxylic acid for the 6(S)-carboxylic acid used in Example 10 and using the procedure described therein, there was obtained a corresponding amount of the title compound.

EXAMPLE 12

Preparation of 6(R)-[2-[8(S)-(2,2-Dimethylbutyryloxy)-6(S)-(N,N-dimethyl)aminocarbonyl-2(S) methyl-1,2,6,7,8,8a(R)-hexahydronaphthyl-1(S)]ethyl]-4(R)-hydroxy-3,4,5,6 -tetrahydro 2H-pyran 2-one

To a stirred solution of 6(R)-[2-[8(S)-(2,2-dimethylbutyryloxy) 6(S)-carboxy-2(S)-methyl-1,2,6,7,8,8a (R)-hexahydronaphthyl-1(S)]ethyl]-4(R)-hydroxy-3,4,5,6-tetrahydro-2H-pyran-2-one (100 mg) in CH.sub.2 Cl.sub.2 (1 mL) cooled to 0.degree. C. and maintained under N.sub.2 was added dropwise a solution of carbonyl diimidazole (39 mg) in CH.sub.2 Cl.sub.2 (1 mL). After stirring for 1 hour at 0.degree. C., the mixture was treated with dimethylamine hydrochloride (20 mg) and stirred for an additional 30 minutes. Then the mixture was partitioned between EtOAc and 1N HCl. The organic phase was separated, washed with aqueous NaHCO.sub.3 and saturated brine, dried (Na.sub.2 SO.sub.4), filtered and evaporated in vacuo to afford a residual oil. Chromatography of this oil on silica gel using a gradient of 1 5% CH.sub.30 H in CH.sub.2 Cl.sub.2 as eluant afforded the title compound as a solid, mp 148.degree.-160.degree. C. after recrystallation from EtOAc-hexane.

Anal. Calc'd for C.sub.27 H.sub.41 N).sub.6 : C, 68.18; H, 8.69; N, 2.94. Found: C, 67.95; H, 8.97; N, 3.06.

EXAMPLE 13

Preparation of 6(R)-[2-[8(S)-(2,2-dimethylbutyryloxy)-6(S)-(N,N-diethyl)aminocarbonyl-2(S)-methyl-1,2,6,7,8,8a(R)-hexahydronaphthyl-1(S)]ethyl]-4(R)-hydroxy-3,4,5,6 -tetrahydro-2H-pyran-2-one

To a stirred solution of 6(R)-[2-[8(S)-(2,2-dimethylbutyryloxy)-6(S)-carboxy-2(S)-methyl-1,2,6,7,8, 8a (R)-hexahydronaphthyl-1(S)]ethyl]-4(R)-hydroxy-3,4,5,6-tetrahydro-2H-pyra n-2-one

To a stirred solution of 6(R)-[2-[8(S)-(2,2-dimethylbutyryloxy)-6(S)-carboxy-2(S)-methyl-1,2,6,7,8, 8a (R)-hexahydronaphthyl-1(S)]ethyl]-4(R)-hydroxy-3,4,5,6-tetrahydro-2H-pyra n-2-one (100 mg) in CH.sub.2 Cl.sub.2 (1.5 mL) cooled to 0.degree. C. and maintained under N.sub.2 was added triethylamine (31.3 ml). After 15 minutes, isobutyl chloroformate (29.4 ml) was added and, after an additional 15 minutes, diethylamine (23.7 ml) was added. The resulting mixture was stirred at 0.degree. C. for 30 minutes and then washed with 1N HCl followed by aqueous NaHCO.sub.3. The organic phase was separated, dried (Na.sub.2 SO.sub.4), filtered and evaporated in vacuo to afford a residual oil. Chromatography of this oil on silica gel using a gradient of 1-5% CH.sub.30 H in CH.sub.2 Cl.sub.2 as eluant afforded the title compound as a solid, mp 154.degree.-155.degree. C. after recrystallization from EtOAc hexane.

Anal. Calc'd for C.sub.29 H.sub.45 NO.sub.6 : C, 69.15; H, 9.01; N, 2.78. Found: C, 68.85; H, 9.09; N, 2.63.

EXAMPLE 14

Preparation of 6(R)-[2-[8(S)-(2,2-Dimethylbutyryloxy)-6(S)-propylaminocarbonyl-2(S)-methy l-1,2,6,7,8,8a(R)-hexahydronaphthyl-1(S)]ethyl]-4(R)-hydroxy-3,4,5,6-tetrah ydro-2H-pyran-2-one

By substituting an equimolar amount of n-propylamine for the diethylamine used in Example 13 and using the procedure described therein, there was obtained the title compound as a colorless solid, mp 96.degree.-105.degree. C.

EXAMPLE 15

Preparation of 6(R)-[2-[8(S)-(2,2-Dimethylbutyryloxy)-6(S)-benzylaminocarbonyl-2(S)-methy l-1,2,6,7,8,8a(R)-hexahydronaphthyl-1(S)]ethyl]-4(R)-hydroxy-3,4,5,6-tetrah ydro-2H-pyran-2-one

By substituting an equimolar amount of benzylamine for the diethylamine used in Example 13 and using the procedure described therein, there was obtained the title compound as a viscous oil.

EXAMPLE 16

Preparation of 6(R)-[2-[8(S)-(2,2-Dimethylbutyryloxy)-6(S)-(2-hydroxyethyl)aminocarbonyl- 2(S)-methyl-1,2,6,7,8,8a(R)-hexahydronaphthyl-1(S)]ethyl]-4(R)-hydroxy-3,4, 5,6-tetrahydro-2H-pyran-2-one

By substituting an equimolar amount of 2-hydroxyethylamine for the diethylamine used in Example 13 and using the procedure described therein, there was obtained the title compound as a viscous oil.

EXAMPLE 17

Preparation of 6(R)-[2-[8(S)-(2,2-Dimethylbutyryloxy)-6(S)-phenylaminocarbonyloxymethyl-2 (S)-methyl-1,2,6,7,8,8a(R)-hexahydronaphthyl (S)]ethyl]-4(R)-hydroxy-3,4,5,6-tetrahydro-2H-pyran-2-one

To a stirred solution of 6(R)-[2-[8(S)-(2,2-dimethylbutyryloxy) 6(S)-hydroxymethyl-2(S)-methyl-1,2,6,7,8,8a(R)-hexahydronaphthyl-1(S)]ethy l]-4(R)-hydroxy-3,4,5,6-tetrahydro-2H-pyran-2-one (80 mg, 0.184 mmol) in sieve dried pyridine (3 mL) was added phenyl isocyanate (22 mg, 0.184 mmol). The resulting solution was stirred at room temperature for 72 hours and then was evaporated in vacuo to provide an oily residue. The residue was partitioned between CHCl.sub.3 (125 mL) and 0.1N HCl (25 mL). The organic phase was separated, washed with 0.1N HCl (2.times.25 ml) and saturated brine (25 mL), dried (Na.sub.2 SO.sub.4), filtered and evaporated in vacuo to give crude product. Chromatography of the crude product on silica gel using CHCl.sub.3 -CH.sub.30 H (98:2, v:v) as eluant afforded the title compound as a colorless gum which solidified upon trituration with hexane, mp 115.degree.-119.degree. C.

Anal. Calc'd for C.sub.32 H.sub.43 NO.sub.7 : C,69.41; H, 7.83; N, 2.53. Found: C,69.51; H, 7.95; N, 2.67.

EXAMPLE 18

Preparation of 6(R)-[2-[8(S)-(2,2-Dimethylbutyryloxy)-2(S)-methyl-6(S)-(N,N-dimethyl)amin ocarbonyl-1,2,3,4,4a(S),5,6,7,8,8a(S)-decahydronaphthyl-1(S)]ethyl]4(R)-hyd roxy-3,4,5,6-tetrahydro-2H-pyran-2-one

(a) 6(R)-[2-[8(S)-hydroxy-2(S-methyl-6(S)-benzyloxymethoxymethyl-1,2,3,4,4a(S) ,5,6,7,8,8a(S)-decahydronaphthyl-1(S)]-ethyl]-4(R)-tert-butyl-dimethylsilyl oxy) 3,4,5,6-tetrahydro-2H-pyran-2-one (18a)

To a stirred solution of compound 2c (9.7 g, 21.3 mmol) and diisopropylethylamine (10 mL, 57.4 mmol) in CH.sub.2 Cl.sub.2 (25 mL) cooled to 0.degree. C. was added dropwise a solution of benzyl chloromethyl ether (3.76 g, 24 mmol) in CH.sub.2 Cl.sub.2 (10 mL). The resulting mixture was stirred at 0.degree. C. for 10 minutes, allowed to warm to room temperature, stirred at room temperature for 22 hours and then poured into ice water. The heterogeneous mixture was extracted with diethyl ether. The organic phase was separated, washed successively with dilute HCl, water, aqueous NaHCO.sub.3 and water, dried (Na.sub.2 SO.sub.4), filtered and evaporated in vacuo to afford a residue which was purified by flash chromatography on silica gel. Elution with CH.sub.2 Cl.sub.2 acetone (50:1; v:v) removed the impurities. Continued elution with CH.sub.2 Cl.sub.2 acetone (20:1: V:V) provided the title compound as a viscous oil; 1.sub.H nmr (CDCl.sub.3) .delta. 0.82 (3H, d, J=7 Hz), 0.88 (9H, s), 2.6 (2H, m), 2.70 (H, d, J=6 Hz), 3.75 (2H, m), 4.0 (H, m), 4.28 (H, m), 4.60 (H, d, J=12 Hz), 4.62 (H, d, J=12 Hz), 4.66 (H, m), 4.78 (H, d, J=6 Hz), 4.81 (H, d, J=6 Hz), 7.3 (5H, m).

(b) 6(R)-[2-[8(S)-(2,2-Dimethylbutyryloxy)-2(S)-methyl-6(S)-benzyloxymethoxyme thyl-1,2,3,4,4a (S),5,6,7,8,8a(S)-decahydronaphthyl-1(S)]ethyl]-4(R)-(tert-b utyldimethylsilyloxy)-3,4,5,6-tetrahydro-2H-pyran-2-one (18b)

Powdered lithium bromide (6.4 g, 74 mmol) was added under N.sub.2 to a stirred mixture of 2,2-dimethylbutyryl chloride (4.97 g, 37 mmol) in pyridine (100 mL) and the resulting mixture was stirred and warmed to 40.degree. C. until a clear solution was obtained. To the resulting solution was added 4 dimethylaminopyridine (0.3 g, 2.45 mmol) and a solution of 18a (7.25 g, 13 mmol) in pyridine (30 mL). The resulting mixture was stirred and heated at 90.degree. C. for 3.5 hours, cooled to room temperature,

poured into ice water and extracted with diethyl ether. The organic phase was separated, washed with dilute HCl, aqueous NaHCO.sub.3 and saturated brine, dried (Na.sub.2 SO.sub.4), filtered and evaporated in vacuo to give an oily residue which was purified by flash chromatography on silica gel. Elution with CH.sub.2 Cl.sub.2 acetone (50:1; v:v) afforded the title compound as a viscous oil; 1.sub.H nmr (CDCl.sub.3) .delta. 0.82 (3H, d, J=7 HZ), 0.83 (3H, t, J=7 Hz), 0.88 (9H, s), 1.14 (3H, s), 1.15 (3H, s), 2.67 (2H, m), 3.39 (H, d of d, J=10, 6 Hz), 3.86 (H, t, J=10 Hz), 4.27 (H, m), 4.54 (H, d, J=16 Hz), 4.61 (H, d, J=16 HZ), 4.74 (2H, S), 5.13 (H, m , 7.32 (5H, m).

(c) 6(R)-[2-[8(S)-(2,2-Dimethylbutyryloxy)-2(S)-methyl-6(S)-hydroxymethyl-1,2, 3,4,4a(S),5,6,7,8,8a (S)-decahydronaphthyl (S)]ethyl]-4(R)-(tert-butyldimethylsilyloxy)-3,4,5,6-tetrahydro-2H-pyran-2 -one (18c)

A mixture of compound 18b (6.1 g, 8.85 mmol), 10% Pd/C (0.5 g) and acetic acid (3 drops) in isopropanol (200 mL) was hydrogenated in a Paar apparatus for 4 hours. The resulting mixture was treated with powdered NaHCO.sub.3 (1 g), stirred for 15 minutes and filtered. The filtrate was evaporated in vacuo to provide a residue which was dissolved in toluene (100 mL). The resulting solution was evaporated in vacuo to provide a residue which again was dissolved in toluene (100 mL). Evaporation of this solution in vacuo gave a residue which crystallized from diethyl ether-hexane to provide the title compound as a colorless solid, mp 70.degree.-71.degree. C.; 'H nmr (CDCl.sub.3) .delta. 0.82 (3H, d, J=7 Hz), 0.83 (3H, t, J=7 Hz), 0.87 (9H, s), 1.15 (3H, s), 1.16 (3H, s), 2.66 (2H, m), 3.55 (H, m), 3.78 (H, m), 4.28 (H, m), 4.65 (H, m), 5.14 (H, m).

Anal. Cal'd for C.sub.31 H.sub.56 O.sub.6 Si: C, 67.34; H, 10.21. Found C, 67.21; H, 10.35.

(d) 6(R)-[2-[8(S)-(2,2-Dimethybutyryloxy)-2(S)-methyl-6(S)-formyl-1,2,3,4,4a(S),5,6,7,8,8a(S)-decahydronaphthyl-1(S)]-ethyl]-4(R)-(tert-butyldimethylsily loxy) 3,4,5,6-tetrahydro-2H-pyran-one (18d)

To a stirred solution of oxalyl chloride (152 mg, 1.2 mmol) in CH.sub.2 Cl.sub.2 (10 mL) cooled at -78.degree. C. was added dimethylsulfoxide (156 mg, 2 mmol) via syringe under N.sub.2. The resulting mixture was stirred at -78.degree. C. for 15 minutes and treated with a solution of compound 18c (383 mg, 0.693 mmol) in CH.sub.2 Cl.sub.2 (5 mL) added dropwise. The resulting mixture was stirred at -78.degree. C., for 30 minutes, treated with triethylamine (253 mg, 2.5 mmol), stirred for an additional 10 minutes at -78.degree. C. warmed to room temperature, poured into ice water and extracted with diethyl ether. The organic extract was washed with aqueous NaHCO.sub.3 and water, dried (Na.sub.2 SO.sub.4), filtered and evaporated in vacuo to provide the title compound as a pale yellow oil; 1.sub.H nmr (CDCl.sub.3) .delta. 0.83 (3H, d, J=7 Hz), 0.83 (3H, t, J=7 Hz), 0.89 (9H, s), 1.10 (3H, s), 1.12 (3H, s), 2.58 (2H, m), 4.28 (H, m), 4.55 (H, m), 5.20 (H, m), 9.63 (H, s).

(e) 6(R)-[2-[8(S)-(2,2-Dimethylbutyryloxy)-2(S)-methyl-6(S)-carboxy-1,2,3,4,4a (S),5,6,7,8,8a(S)-decahydronaphthyl-1(S)]ethyl]-4(R)-(tert-butyldimethylsil yloxy) 3,4,5,6-tetrahydro-2H-pyran-2-one (18e)

To a stirred mixture of compound 18d (380 mg, 0.69 mmol) and sulfamic acid (97 mg, 1 mmol) in THF water (5:1; v:v; 24 mL) cooled at 0.degree. C. was added sodium chlorite (113 mg, 80% active, 1 mmol) in one portion. The resulting mixture was stirred at 0.degree. C. for 10 minutes, warmed to room temperature and stirred for 2 hours. Then the mixture was poured into aqueous sodium thiosulfate and extracted with diethyl ether. The organic extract was washed with water, dried (Na.sub.2 SO.sub.4), filtered and evaporated in vacuo to provide a residue which was purified by flash chromatography on silica gel. Elution with CH.sub.2 Cl.sub.2 acetone (10:1; v:v) afforded the title compound as a colorless gum; 1.sub.H nmr (CDCl.sub.3) .delta. 0.83 (3H, t, J=7 Hz), 0.84 (3H, d, J=7 Hz), 0.89 (9H, s), 1.10

(3H, s), 1.12 (3H, s), 2.15 (H, d, J=9 Hz), 2.60 (2H, m), 2.68 (2H, m) 4.30 (H, m), 4.58 (H, m), 5.68 (H, m).

(f) 6(R)-[2-[8(S)-(2,2-Dimethylbutyryloxy)-2(S)-methyl-6(S)-chlorocarbonyl-1,2 ,3,4,4a(S),5,6,7,8,a(S)-decahydronaphthyl-1(S)]ethyl]-4(R)-(tert-butyldimet hylsilyloxy) 3,4,5,6-tetrahydro-2H-pyran 2-one (18f)

DMF (1 drop) was added to a magnetically stirred solution of compound 18e (56 mg, 0.1 mmol) and oxalyl chloride (19 mL, 0.22 mmol) in benzene (2 mL) The resulting mixture was stirred at ambient temperature for 2 hours to provide a heterogeneous mixture which was decanted. Evaporation of the decantate in vacuo gave the title compound as a pale yellow oil; 1.sub.H nmr (CDCl.sub.3 .delta. 0.072 (3H, s), 0.082 (3H, s), 0.88 (9H, s), 1.13 (3H, s), 1.16 (3H, s), 3.02 (H, m), 4.28 (H, m), 4.55 (H, m), 5.20 (H, m).

(g) 6(R)-[2-[8(S)-2,2-Dimethylbutyryloxy)-2(S)-methyl-6(S)-(N,N dimethyl)aminocarbonyl-1,2,3,4,4a (S),5,6,7,8,8a(S)-decahydronaphthyl-1(S)] ethyl]-4(R)-(tert-butyl dimethylsilyloxy) 3,4,5,6-tetrahydro-2H pyran 2-one (18g)

Dimethylamine was bubbled slowly into a magnetically-stirred solution of compound 18f (58 mg, 0.1 mmol) in diethyl ether (10 mL) until the precipitation of dimethylammonium chloride ceased. Then the mixture was stirred at ambient temperature for 18 hours and filtered. Evaporation of the filtrate in vacuo provided a residual oil which was chromatographed on silica gel (230-400 mesh, 3.times.15 cm). Elution with isopropanol-hexane (1:5; v:v) afforded the title compound as a colorless oil; 1.sub.H nmr (CDCl.sub.3 .delta. 0.073 (3H, s), 0.084 (3H, s), 0.88 (9H, s), 1.09 (6H, s), 2.89 (3H, s), 2.95 (3H, s), 4.30 (H, m), 4.56 (H, m), 5.14 (H, m).

(h) 6(R)-[2-[8(S)-(2,2-Dimethylbutyryloxy)-2(S)-methyl-6(S)-(N,N dimethyl)aminocarbonyl-1,2,3,4,4a (S),5,6,7,8,8a(S) decahydronaphthyl-1(S)]-ethyl-4(R)-hydroxy-3,4,5,6-tetrahydro-2H-pyran-2-o ne (18h)

To a stirred solution of compound 18g (78 mg, 0.13 mmol) and acetic acid (30mL, 0.525 mmol) in THF (10 mL) was added tetra-n-butylammonium fluoride (1M in THF, 394 mL, 0.394 mmol . After stirring at ambient temperature for 18 hours, additional tetra-n-butylammonium fluoride (394 mL) and acetic acid (30 mL) were added to the mixture and stirring was continued for 24 hours. Evaporation of the resulting solution in vacuo gave a residue which was partitioned between ether (50 mL) and water (20 mL). After separating the phases, the aqueous phase was extracted with diethyl ether 50 mL . The diethyl ether extracts were combined, washed with aqueous NaHCO.sub.3 and saturated brine, dried (MgSO.sub.4) and evaporated in vacuo to provide a viscous oil which was chromatographed on silica gel (230 400 mesh, 3.times.15 cm). Elution with isopropanol-hexane (1:3; v:v) afforded the title compound as a colorless solid, mp 186.degree.-187.degree. C. after recrystallization from diethyl ether hexane; 1.sub.H nmr (CDCl.sub.3) .delta. 1.11 (6H, s), 2.88 (3H, s), 2.96 (3H, s), 4.37 (H, m), 4.54 (H, m), 5.17 (H, m).

Anal. Calc'd for C.sub.27 H.sub.45 NO.sub.6 : C, 67.61; H, 9.46; N, 2.92 Found: C, 67.26; H, 9.64; N, 2.77.

EXAMPLE 19

Preparation of 6(R)-[2-[8(S)-(2,2-Dimethylbutyryloxy)-2(S)-methyl-6(S)-aminocarbonyl-1,2, 3,4,4a (S),5,6,7,8,8a(S)-decahydronaphthyl-1(S)]ethyl]-4(R)-hydroxy-3,4,5,6- tetrahydro-2H-pyran-2-one

(a) 6(R)-[2-[8(S)-(2,2-Dimethylbutyryloxy)-2(S)-methyl-6(S)-aminocarbonyl-1,2, 3,4,4a(S),5,6,7,8,8a (S)-decahydronaphthyl-1(S)]ethyl]-4(R)-(tert-butyldimet hylsilyloxy)-3,4,5,6-tetrahydro-2H-pyran-2-one (19a)

By substituting an equimolar amount of ammonia for the dimethylamine used in Step (g) of Example 18 and using the procedure described therein, there was obtained the title compound as a colorless oil; 1.sub.H nmr (CDCl.sub.3) .delta. 0.073 (3H, s), 0.082 (3H, s), 0.883 (9H, s), 1.14 (6H, s), 4.28 (H, m), 4.56 (H, m), 5.08 (H, m), 5.28 (H, bs), 5.52 (H, bs).

(b) 6(R)-[2-[8(S)-(2,2-Dimethylbutyryloxy)-2(S)-methyl-6(S)-aminocarbonyl-1,2, 3,4,4a(S),5,6,7,8,8a (S)-decahydronaphthyl-1(S)]ethyl]-4(R)-hydroxy-3,4,5,6- tetrahydro-2H-pyran-2-one (19b)

By substituting an equimolar amount of compound 19a for compound 18g used in Step (h) of Example 18 and using the procedure described therein, there was obtained the title compound as a colorless solid, mp 116.degree.-118.degree. C.; 1.sub.H nmr (CDCl.sub.3) .delta. 0.82 (3H, d, J=7 Hz), 0.83 (3H, t, J=7 Hz), 1.14 (3H, s), 1.15 (3H, s), 4.36 (H, m), 4.56 (H, m), 5.10 (H, m), 5.22 (H, bs), 5.50 (H, bs).

Anal Calc'd for C.sub.25 H.sub.41 NO.sub.6 : C,66.49; H, 9.15; N, 3.10. Found: C,66.79; H, 9.35; N, 2.86.

EXAMPLE 20

Preparation of 6(R)-[2-[8(S)-(2,2-Dimethylbutyryloxy)-2(S)-methyl-6(S)-ethoxycarbonyl-1,2 ,3,4,4a (S),5,6,7,8,8a(S)-decahydronaphthyl-1(S)]ethyl]-4(R)-hydroxy-3,4,5,6 -tetrahydro-2H-pyran-2-one

(a) 6(R)-[2-[8(S)-(2,2-Dimethylbutyryloxy)-2(S)-methyl-6(S)-ethoxycarbonyl-1,2 ,3,4,4a(S),5,6,7,8,8a (S)-decahydronaphthyl-1(S)]ethyl]-4(R)-(tert-butyldime thylsilyloxy)-3,4,5,6-tetrahydro-2H-pyran-2-one (20a)

To a stirred solution of compound 18f (120 mg, 0.205 mmol) in pyridine (5 mL) was added 4-dimethylaminopyridine (25 mg, 0.205 mmol) and EtOH (33 mg, 0.72 mmol). The resulting mixture was stirred at ambient temperature for 4 days and then was partitioned between cold 3N HCl and ether. The organic phase was separated, washed with 3N HCl (until pH 4 was sustained in the aqueous phase), washed with aqueous NaHCO.sub.3, dried (Na.sub.2 SO.sub.4) and filtered. Evaporation of the filtrate in vacuo gave an oily resiue which was purified by flash chromatography on silica gel. Elution with CH.sub.2 Cl.sub.2 acetone (95:5; v:v) afforded the title compound as a viscous oil; 1.sub.H nmr (CDCl.sub.3) .delta. 0.88 (9H, s), 1.08 (3H, s), 1.11 (3H, s), 2.14 (H, d, J=12 Hz), 2.5-2.7 (3H, m), 4.0 (H, m), 4.18 (H, m), 4.28 (H, m), 4.55 (H, m), 5.13 (H, m).

(b) 6(R)-[2-[8(S)-(2,2-Dimethylbutyryloxy)-2(S)-methyl-6(S)-ethoxycarbonyl-1,2 ,3,4,4a(S),5,6,7,8,8a (S)-decahydronaphthyl-1(S)]ethyl]-4(R)-hydroxy-3,4,5,6 -tetrahydro-2H-pyran-2-one (20b)

To a stirred solution of compound 20a (38 mg, 0.055 mmol) and acetic acid (26 ml) in THF (1 mL) was added tetra n butylammonium fluoride (1M in THF, 320 mL, 0.32 mmol). The resulting mixture was stirred at room temperature for 20 hours and then poured into cold aqueous NaHCO.sub.3 and extracted with diethyl ether. The organic phase was separated, dried (Na.sub.2 SO.sub.4), filtered and evaporated in vacuo to yield the title compound as a viscous oil; 1.sub.H nmr (CDCl.sub.3) .delta. 0.82 (3H, d, J=7 Hz), 0.83 (3H, t, J=7 Hz), 1.07 (3H, s), 1.11 (3H, s), 2.15 (H, d, J=12 Hz), 2.74 (H, d of d, J=16, 4 Hz), 4.03 (H, m), 4.18 (H, m), 4.37 (H, m), 4.57 (H, m), 5.19 (H, m).

Anal Calc'd for C.sub.27 H.sub.44 O.sub.7 : C, 67.47; H, 9.23. Found: C, 67.73; H, 9.43.

EXAMPLE 21

Preparation of 6(R)-[2-[8(S)-(2,2-Dimethylbutyryloxy)-2(S)-methyl-6(S)-isopropoxycarbonyl -1,2,3,4,4a(S),-5,6,7,8,8a(S)-decahydronaphthyl-1(S)]ethyl]-4(R)-hydroxy-3, 4,5,6-tetrahydro-2H-pyran-2-one

(a) 6(R)-[2-[8(S)-(2,2-Dimethylbutyryloxy)-2(S)-methyl-6(S)-isopropoxycarbonyl -1,2,3,4,4a (S),5,6,7,8,8a(S)-decahydronaphthyl-1(S)]ethyl]-4(R)-(tert-butyl dimethylsilyloxy)-3,4,5,6-tetrahydro-2H-pyran-2-one (21a)

To a stirred solution of compound 18e (140 mg, 0.247 mmol), 4-dimethylaminopyridine (14 mg, 0.112 mmol) and isopropanol (39 mg, 0.67 mmol) in CH.sub.2 Cl.sub.2 (300 .mu.L) cooled to 0.degree. C. was added dropwise a solution of N,N'-dicyclohexylcarbodiimide (76 mg, 0.37 mmol) in CH.sub.2 Cl.sub.2 (500 .mu.L). The resulting mixture was stirred and allowed to come to room temperature overnight. After collecting the precipitated solid, the filtrate was evaporated in vacuo to provide an oilY residue which was purified by flash chromatography on silica gel. Elution with CH.sub.2 Cl.sub.2 - acetone (98:2; v:v) afforded a mixture of the title compound [1.sub.H nmr CDCl.sub.3) .delta. 0.88 (9H, s), 2.68 (2H, m), 4.28 (H, m), 4.55 (H, m), 4.95 (H, m), 5.13 (H, m)]and the acylurea by-product (19 by-product).

(b) 6(R)-[2-[8(S)-(2,2-Dimethylbutyryloxy)-2(S)-methyl-6(S)-isopropoxycarbonyl -1,2,3,4,4a(S),-5,6,7,8,8a(S)-decahydronaphthyl-1(S)]ethyl]-4(R)-hydroxy-3, 4,5,6-tetrahydro-2H-pyran-2-one (19b)

To a stirred solution of the mixture (90 mg) of compounds 19a and 19 by-product and acetic acid (70 L) in THF (2.5 mL) was added tetra-n-butylammonium fluoride (1M in THF, 860 .mu.L, 0.86 mmol). The resulting mixture was stirred at room temPerature for 20 hours and then poured into cold 5 aqueous NaHCO.sub.3 and extracted with diethyl ether. The organic phase was separated, dried (Na.sub.2 SO.sub.4), filtered and evaporated in vacuo to leave an oily residue which crystallized from diethyl ether-hexane to afford the title compound as a solid, mp 160.degree.-161.degree. C; 1.sub.H nmr (CDCl.sub.3) .delta. 0.82 (3H, d, J=7 Hz), 0.83 (3H, t, J=7 Hz), 1.10 (3H, s), 1.13 (3H, s), 1.20 (3H, d, J=6 Hz), 1.22 (3H, d, J=6 Hz), 2.15 (H, d, J=12 Hz), 2.74 (H, d of d, J=18, 6 Hz), 4.35 (H, 4.55 (H, m), 4.95 (H, m , 5.17 (H, m).

Anal Calc'd for C.sub.28 H.sub.46 O.sub.7 : C, 67.98; H, 9.37. Found: C, 68.08; H, 9.62.

EXAMPLE 22

Preparation of 6(R)-[2-[8(S)-(2,2-Dimethylbutyryloxy)-2(S)-methyl-6(S)-(N-cyclohexylamino carbonyl,N-cyclohexyl)aminocarbonyl-1,2,3,4,4a(S),5,6,7,8,8a(S)-decahydrona phthyl-1(S)]ethyl]-4(R)-hydroxy-3,4,5,6-tetrahydro-2H-pyran-2-one

The title compound was isolated as the by product from Step (b) of Example 21 and was purified by recrystallization from diethyl ether hexane which afforded a solid, mp 137.degree.-138.degree. C.; 1.sub.H nmr (CDCl.sub.3) .delta. 1.08 (3H, s), 1.09 (3H, s), 2.60 (H, d of d, J=18, 5 Hz), 2.74 (H, d of d, J=18, 6 Hz), 2.88 (H, m), 3.63 (3H, m), 4.37 (H, m), 4.58 (H, m), 5.16 (H, m).

Anal. Calc'd for C.sub.38 H.sub.62 N.sub.2 O.sub.7 : C,69.26; H, 9.49;N, 4.25. Found: C,68.82; H, 9.70,N, 4.11.

EXAMPLE 23

Preparation of 6(R)-[2-[8(S)-(2,2-Dimethylbutyryloxy)-2(S)-methyl-6(R)-hydroxymethyl-1,2, 3,4,4a (S),5,6,7,8,8 a(S)-decahydronaphthyl-1(S)]ethyl]-4(R)-hydroxy-3,4,5,6-tetrahydro-2H-pyra n-2-one

(a) 6(R)-[2-[8(S)-(2,2-Dimethylbutyryloxy)-2(S)-methyl-6(R)-formyl-1,2,3,4,4a(s),5,6,7,8,8a(s)-decahydronaphthyl-1(S)]ethyl]-4(R)-hydroxy-3,4,5,6-tetrahy dro-2H-pyran-2-one (23a)

To a stirred solution of compound 18d (300 mg, 0 54 mmol) and acetic acid (0.35 mL) in THF (10 mL) was added tetra n butylammonium fluoride (1M in THF, 4.3 mL, 4.3 mmol . The resulting mixture was stirred at room temperature for 15 hours and then poured into cold water and extracted with diethyl ether. The organic phase was separated, washed with aqueous NaHCO.sub.3, dried (Na.sub.2 SO.sub.4, filtered and evaporated in vacuo to provide a residual oil which was purified by chromatography on silica gel. Elution with CH.sub.2 Cl.sub.2 acetone (9:1; v:v) afforded an epimeric mixture of the title compound [1.sub.H nmr (CDCl.sub.3) w 0.85 3H, d, J=7 Hz), 1.18 (3H, s), 5.28 H, m), 9.64 (H, d, J=1 Hz)]and the corresponding 6.alpha.-epimer [1.sub.H nmr (CDCl.sub.3) .delta. 0.83 (3H, d, J=7 Hz), 1.10 (3H, s), 1.12 (3H, s), 5.24 (H, m), 9.60 (H, d, J=1 Hz)], 6(R)-[2-[8(S)-(2,2-dimethylbutyryloxy)-2(S)-methyl-6(S)-formyl-1,2,3,4,4a(S),5,6,7,8,8a(s) deca-hydronaphthyl-1(s)]ethyl]-4(R)-hydroxy-3,4,5,6-tetra-hydro-2H-pyran-2 -one (21 epimer). The mixture of epimers 23a and 23 epimer could be separated by chromatography or used as such in Step (b) below.

(b) 6(R)-[2-[8(S)-(2,2-Dimethylbutyryloxy)-2(S)-methyl-6(R)-hydroxymethyl-1,2, 3,4,4a(S),5,6,7,8,8a (S)-decahydronaphthyl-1(S)]ethyl]-4(R)-hydroxy-3,4,5,6- tetrahydro-2H-pyran-2-one (23b)

By substituting an equimolar amount of the epimeric mixture of 23a and 23 epimer from Step (a) above for compound 2d in Step (e) of Example 2 and using the procedure described therein, there was obtained an epimeric mixture of the title compound and compound 2g, the latter being identical to an authentic sample of 2g prepared as described in Example 2. Separation of this epimeric mixture into pure compounds 23b and 2g could be accomplished by chromatography.

EXAMPLE 24

Preparation of 6(R)-[2-[8(S)-(2,2-Dimethylbutyryloxy)-2(S)-methyl-6(R)-carboxy-1,2,3,4,4a (S),5,6,7,8,8a(S)-decahydronaphthyl-1(S)]ethyl]-4(R)-hydroxy-3,4,5,6-tetrah ydro-2H-pyran-2-one

By substituting an equimolar amount of compound 23a for compound 7a in Step (b) of Example 7 and using the procedure described therein, there was obtained the title compound.

EXAMPLE 25

Preparation of 6(R)-[2-[8(S)-(2,2-Dimethylbutyryloxy)-2(S)-methyl-6(S)-phenylaminocarbony loxymethyl-1,2,3,4,4a(S),5,6,7,8,8a(S)-decahydronaphthyl-1(S)]-ethyl]-4(R)- hydroxy-3,4,5,6-tetrahydro-2H-pyran-2-one

By substituting an equimolar amount of compound 2h for the 6(R)-[2-[8(S)-(2,2-dimethylbutyryloxy)-2 (S)-methyl-6(S)-hydroxymethyl-1,2, 6,7,8,8a(R)-hexahydronaphthyl-1(S)]ethyl]-4(R)-hydroxy-3,4,5,6-tetrahydro-2 H-pyran-2-one in Example 17 and using the procedure described therein, there was obtained the title compound.

EXAMPLES 28-35

Utilizing the general procedure described in Example 8 and starting with the 6-carboxy derivatives

prepared according to the bioconversion reactions of Example 1, the following compounds of the formula (I) with the indicated absolute stereochemistry (AS) at C-6 are prepared from the appropriate diazoalkane:

Compound Number	a	b	c	AS	R	R.sup.1
28	db	--	db	S	CO.sub.2 Me	1,1-dimethyl-propyl
29	db	--	db	R	CO.sub.2 Me	1,1-dimethyl-propyl
30	db	--	db	S	CO.sub.2 iPr	sec-butyl
31	db	--	db	R	CO.sub.2 iPr	sec-butyl

Similarly, starting with the 6-carboxy derivatives which are prepared utilizing the general procedures of Examples 7 and 24, the following compounds of formula (I) with the indicated absolute stereochemistry (AS) at C-6 are also prepared:

Compound Number	a	b	c	AS	R	R.sup.1
32	--	--	--	R	CO.sub.2 iPr	1,1-dimethyl-propyl
33	db	--	--	S	CO.sub.2 Me	1,1-dimethyl-propyl
34	--	db	--	S	CO.sub.2 Me	1,1-dimethyl-propyl
35	--	--	db	R	CO.sub.2 Me	sec-butyl

EXAMPLES 36-42

The following compounds of the formula (I) with the indicated absolute sterochemistry (AS) at C-6 and wherein R is ##STR32## are prepared from the corresponding compounds wherein R is CH.sub.2 OH and in which the 4-hydroxy function of the lactone moiety is protected as a tetrahydropyranyl ether group by a standard acylation reaction utilizing the appropriate acyl halide or anhydride followed by the deprotection of the 4-hydroxy function:

Compound Number

	a	b	c	AS	R	R.sup.1
36	db	--	db	S	##STR33##	sec-butyl
37	db	--	db	S	##STR34##	1,1-dimethylpropyl
38	--	--	--	S	##STR35##	sec-butyl
39	--	--	--	S	##STR36##	1,1-dimethylpropyl
40	db	--	--	R	##STR37##	1,1-dimethylpropyl
41	--	db	--	S	##STR38##	1,1-dimethylpropyl
42	--	--	db	S	##STR39##	sec-butyl

EXAMPLES 43-49

Using the general procedure described in Example 17 and starting with the corresponding compounds wherein R is CH.sub.2 OH, the following compounds of the formula (I) with the indicated absolute stereochemistry (AS) at C-6, and wherein R is ##STR40## and R.sup.5 is NH.sub.2 or a substituted amino moiety, are prepared:

Compound Number	a	b	c	AS	R	R.sup.1
43	db	--	db	R	##STR41##	1,1-methylpropyl
44	db	--	db	S	##STR42##	sec-butyl
45	db	--	--	R	##STR43##	1,1-dimethylpropyl
46	--	db	--	S	##STR44##	1,1-dimethylpropyl

47	--	--	db	S	##STR45##	sec-butyl
48	--	--	--	S	##STR46##	1,1-dimethylpropyl
49	--	--	--	R	##STR47##	sec-butyl

EXAMPLES 50-57

Utilizing the general acylation procedures disclosed in co-pending patent applications Ser. No. 859,524, 859,534, 859,535, all filed May 5, 1986, the following compounds of the formula (I) with the indicated absolute stereochemistry (AS) at C-6 wherein the R.sup.1 substituent is elaborated are prepared from the 6-carboxy, 6-alkoxycarbonyl, the protected 6-hydroxymethyl and the 6-acyloxymethyl derivatives.

Compound Number	a	b	c	AS	R	R.sup.1
50	db	--	db	S	CH.sub.2	OH cyclohexyl-
51	db	--	db	R	CH.sub.2	OH HOCH.sub.2
52	db	--	db	S	CO.sub.2	H CH.sub.3 COCH.sub.2
53	--	--	--	S	CO.sub.2	H cyclobutyl-
54	--	--	--	R	CH.sub.2	OH HOCH.sub.2 CH.sub.2 C(CH.sub.3).sub.2
55	db	--	--	R	CH.sub.2	OH HO(CH.sub.2).sub.3 C(CH.sub.3).sub.2
56	--	db	--	S	CO.sub.2	CH.sub.3 CH.sub.3 COCH.sub.2 CH.sub.2 C(CH.sub.3).sub.2
57	--	--	db	S	##STR48##	cyclohexyl

EXAMPLE 58-62

Utilizing the methodology of Example 3 and the procedures disclosed in copending patent applications Ser. No. 131695 filed Dec. 12, 1987 and Ser. Nos. 161530, 161529 all filed Feb. 29, 1988 and the hydrogenation procedure in U.S. Pat. No. 4,444,784 the following compounds of the formula (I) with the indicated stereochemistry (AS) at C-6 are prepared.

Compound

Number	a	b	c	AS	R	R.sup.1
58	db	--	db	S	CH.sub.3	CHOH 1,1-methylpropyl
59	db	--	db	R	CH.sub.3	CHOH 1,1-methylpropyl
60	db	--	db	S	CH.sub.3	CHOH sec-butyl
61	db	--	db	R	CH.sub.3	CHOH sec-butyl
62	db	--	--	R	CH.sub.3	CHOH 1,1-methylpropyl

EXAMPLE 63

Preparation of Ammonium Salts of Compounds II

The lactone 2h (1.0 mmol) from Example 2 is dissolved with stirring in 0.1N NaOH (1.1 mmol) at ambient temperature. The resulting solution is cooled and acidified by the dropwise addition of 1N HCl. The resulting mixture is extracted with diethyl ether and the extract washed with brine and dried (MgSO.sub.4). The MgSO.sub.4 is removed by filtration and the filtrate saturated with ammonia (gas to give a gum which solidified to provide the ammonium salt.

EXAMPLE 64

Preparation of Alkali and Alkaline Earth Salts of Compounds II

To a solution of 42 mg of lactone 2h from Example 2 in 2 ml of ethanol is added 1 ml of aqueous NaOH (1 equivalent). After one hour at room temperature, the mixture is taken to dryness in vacuo to yield the desired sodium salt.

In like manner, the potassium salt is prepared using one equivalent of potassium hydroxide, and the calcium salt, using one equivalent of CaO.

EXAMPLE 65

Preparation of Ethylenediamine Salts of Compounds II

To a solution of 0.50 g of the ammonium salt from Example 63 in 10 ml of methanol is added 75 ml of ethylenediamine. The methanol is stripped off under vacuum to obtain the desired ethylenediamine salt.

EXAMPLE 66

Preparation of Tris(hydroxymethyl)aminomethane Salts of Compounds II

To a solution of 202 mg of the ammonium salt from Example 63 in 5 ml of methanol is added a solution of 60.5 mg of tris(hydroxymethyl) aminomethane in 5 ml of methanol. The solvent is removed in vacuo to afford the desired tris(hydroxy methyl)aminomethane salt.

EXAMPLE 67

Preparation of L-Lysine Salts of Compounds II

A solution of 0 001 mole of L-lysine and 0.0011 mole of the ammonium salt from Example 63 in ml of 85% ethanol is concentrated to dryness in vacuo to give the desired L-lysine salt.

Similarly prepared are the L-arginine, L-ornithine, and N-methylglucamine salts.

EXAMPLE 68

Preparation of Tetramethylammonium Salts of Compounds II

A mixture of 68 mg of ammonium salt from Example 63 in 2 ml of methylene chloride and 0.08 ml of 24% tetramethylammonium hydroxide in methanol is diluted with ether to yield the desired tetramethylammonium salt.

EXAMPLE 69

Preparation of Methyl Esters of Compounds II

To a solution of 400 mg of lactone 2h from Example 2 in 100 ml of absolute methanol is added 10 ml 0.1 M sodium methoxide in absolute methanol. This solution is allowed to stand at room temperature for one hour, then is diluted with water and extracted twice with ethyl acetate. The organic phase is separated, dried (Na.sub.2 SO.sub.4), filtered and evaporated in vacuo to yield the desired methyl ester.

In like manner, by the use of equivalent amounts of propanol, butanol, isobutanol, t-butanol, amylalcohol, isoamylalcohol, 2-dimethylaminoethanol, benzylalcohol, phenethanol, 2-acetamidoethanol and the like, and employing the corresponding alcohol as solvent, the corresponding esters are obtained.

EXAMPLE 70

Preparation of Free Dihydroxy Acids

The sodium salt of the compound II from Example 64 is dissolved in 2 ml of ethanol-water (1:1; v:v) and added to 10 ml of 1N hydrochloric acid from which the dihydroxy acid is extracted with ethyl acetate. The organic extract is washed once with water, dried (Na.sub.2 SO.sub.4), and evaporated in vacuo with a bath temperature not exceeding 30.degree. C. The dihydroxy acid derivative derived slowly reverts to the corresponding, parent lactone on standing. The dihydroxy acid can be maintained by increasing the pH above 7.0.

EXAMPLE 71

As a specific embodiment of a composition of this invention, 20 mg of lactone 2h from Example 2, is formulated with sufficient finely divided lactose to provide a total amount of 580 to 590 mg to fill a size 0, hard gelatin capsule.

* * * * *

Images